An Overview of the Herbal Treatment of Viral Diseases

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By

Sukirti Upadhyay and Prashant Upadhyay

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ABSTRACT

The virus is a link between nonliving and living. Due to its ambiguous nature, these can survive in various extreme environmental conditions and it is hard for any medicament to cope up with them. Natural immunity, vaccines, and antiviral medicines are available to mankind against viral exploration but synthetic antiviral agents are toxic and have side effects. So, there is a new hope for the ancient system of medicine which advocates herbs for curing diseases by enhancing immunity. In this book, many herbs that are scientifically proven for anti-viral effects are discussed along with their phytoconstituents and mechanism of action.

LIST OF ABBREVIATIONS

AD:	Alzheimer's disease
APC:	Antigen presenting cell
ADMET:	Absorption distribution metabolism excretion toxicity
BBB:	Blood-brain barrier
CC50:	Cytotoxic concentration 50
CD4:	Cluster of Differentiation 4
COVID:	Corona Virus Disease
DNA:	Deoxynucleic acid
EC50:	Half maximal effective concentration
FAS:	full analysis test
HPLC:	high-performance liquid chromatography
HeLa Cells:	Henrietta Lacks
HSV:	Herpes simplex virus
HIV:	Human Immunodeficiency Virus
IFN:	Interferon
Kb:	Kilobase
MHC:	Major Histocompatibility Complex
nm:	nanometer
PPS:	Per protocol test
PCR:	Protein chain reaction
RNA:	Ribonucleic acid
SARS:	Severe acute respiratory syndrome
SI:	Selectivity Index
T.i.d.:	Ter in die, three times in a day
T cell:	Thymus cell
TMV:	Tobacco mosaic virus
WHV:	Woodchuck Hepatitis Virus

CHAPTER 1

CHARACTERISTICS OF VIRUS, SYNTHETIC MEDICINES AND VACCINES FOR THEIR CONTROL, MODELS FOR ANTIVIRAL SCREENING

DR. SUKIRTI UPADHYAY

Viruses are ubiquitous in all living environments and most likely have existed simultaneously with the evolution of living cells. Since viruses never end up as fossils, their origin is unclear. To learn more about their origins, molecular techniques are employed. [1] Furthermore, on rare occasions, viral genetic material merges with the host organisms' germline, allowing the viruses to be vertically transferred to the next generation of hosts. Paleo-virologists trace back to the host generation to find the source of origin, that date back millions of years. [2]

A virus is a combination of living and non-living things. It never transports RNA and DNA simultaneously. We'll discuss a variety of viral infections in this book, along with herbal and spice remedies for prevention. Recently India used to fight the coronavirus with a variety of herbal extracts. Viral agents cause both serious diseases like COVID-19 and less serious ones like Influenza. Viruses are resistant to traditional antibiotics and can only be cured by the immunity of a single cell. One of the primary causes of illness worldwide is viral infections, particularly in light of the rising rates of urbanization, migration, and international travel. An estimated 1031 viruses exist in the world. [3] Out of 1031 viruses on Earth, most of which are phages that attack bacteria. Environmental viral populations exhibit a great diversity, as demonstrated by metagenomic studies. One kilogram of marine

sand may contain a million different viral genotypes, whereas 200 litres of saltwater is estimated to contain 5000 different viral genotypes. [4]

Some similar agents to virus found in nature are described below: -

RNA Molecules

RNA molecules are infectious but are devoid of protein coat, are not categorized as virus. They are classified as sub-viral agents because they have numerous similar characteristics with virus.

Viroids

Important plant pathogens are viroids. They engage with the host cell and replicate by using its machinery, but Proteins are not encoded by them. The RNA genome of the delta virus that causes human hepatitis contains viroids, but because it cannot make its protein coat, it uses one that was obtained from the hepatitis B virus. As a result, the virus has flaws. The hepatitis delta virus can replicate its DNA after it has entered the host cell, but it always needs the hepatitis B virus to make a protein coat. The Sputnik virophage depends on the mimivirus, which infects the protozoan *Acanthamoeba castellanii*, similarly. Because these viruses, dubbed "satellites," depend on the existence of other viral species in the host cell, they could be evolutionary intermediates of viroids and viruses.

Origin of Virus

These theories are assumed about the origin of the Virus: -

1. **Regressive Theory/Reduction Theory/Degeneracy Theory**

According to this theory, viruses are parasites that depend upon bigger cells for survival. The genes which were not needed for parasitic achievements were gradually lost. This feature is also present in some lower bacteria like Chlamydia and Rickettsia.

2. **Cellular origin Theory/Escape Theory/Vagrancy Theory**

According to this theory, certain viruses might have developed from fragments of RNA or DNA that "escaped" from a larger organism's genes.

The DNA that escaped may have originated from transposons, which are DNA molecules that duplicate and move to dissimilar locations within a cell's genes, or from plasmids, which are bare DNA fragments that are mobile between cells. Transposons are examples of mobile genetic elements that were formerly known as "jumping genes," and they may have originated some viruses. Barbara McClintock discovered them in maize in 1950. This is also referred to as the "escape theory" or the "vagrancy theory."

3. Co-evolution Theory

According to the 'virus-first hypothesis,' as it is also known, viruses might have originated from intricate protein and nucleic acid molecules around the same time that cells initially appeared on Earth (as proved by the Stanley Miller experiment) but they were not able to survive on their own and have been dependent on cellular life for billions of years.

It would seem that co-infections with viruses are not unusual in nature, nor in the lab, given the mounting body of evidence demonstrating the pervasiveness of endogenous viral infections in all spheres of life. Nevertheless, they have rarely been thoroughly analysed for possible viral interactions, and most of the interactions that have been reported have been discovered accidentally. Unquestionably, not every viral species will interact with one another through co-infection. However, given that many viruses cause major host alterations, it seems likely that virus-virus interactions occur frequently and may be important to consider when considering viral pathophysiology and evolution [1]

As such, in this book, we divide known and potential virus-virus interactions into three categories: [5]

I. Straight forward interactions
   a. Helper-dependent viruses
   b. Super infection exclusion
   c. Pseudo-type viruses
   d. Genomic recombination
   e. Heterologous transactivation
   f. Embedded viruses
II. Interactions with the Environment

a. Altered receptor expression
b. Modification of the interferon-induced antiviral state
c. Indirect transactivation of genes
d. Heterologous activation of pro-drugs
e. Breakdown of physical barriers

III. Immune effects

a. Heterologous immunity
b. Antibody-dependent progression of infection
c. Induction of autoimmunity
d. Altered immune cell activation

These all interactions paved the pathway for viral residence and infection in the host cell.

As the virus embeds in tissue it may be inert for a lifetime or fatal.

An example of its fatality: Virus -invasion and residence in host brain cells

The course and clinical results of a viral CNS infection are significantly influenced by T cells. According to the information in this book, the following series of events could be brought on by an acute viral infection.

The most frequent method by which the virus penetrates the central nervous system (CNS) after host invasion and a brief initial replication cycle is through hematogeneous dissemination. Once the virus has penetrated the blood-brain barrier, it multiplies in brain cells, infecting CNS cells and stimulating the local microglia population. Furthermore, MHC antigens are expressed by CNS cells due to local IFN-alpha/beta production, and microglial cells start phagocytosing cellular debris that accumulates as a result of viral cytopathogenic effects. [6]

Microglia become more activated following phagocytosis; they produce chemokines, up-regulate MHC molecules, and develop the ability to present antigens. Adhesion molecules on nearby blood brain barrier (BBB) endothelial cells will start to upregulate as a result. After activated T lymphocytes transmigrate across the BBB, they interact with the APC and present the relevant peptides in relation to MHC antigens. CD8+ T

lymphocytes appear to be among the first mononuclear cells to enter the infected tissue.

Undoubtedly, Natural killer cells have a significant role in both their induction and attraction. After being infected by a virus, these cells release IFN gamma, a cytokine that activates CD8+T cells and shifts the immune response so that TH1-type CD4+T cells dominate it. TH1 CD4+T cells that penetrate tissue produce interaction with nearby APC after CD8+T cells. Consequently, there is a marked upregulation of MHC molecules and an increased release of chemotactic and poisonous chemicals.

As a result, more and more inflammatory cells, such as macrophages and microglia, as well as plasma cells that secrete antibodies, are drawn to the virus infection site. The majority of all cells have reached the ultimate stage of differentiation. Clinical results are determined by the stability and fine-tuning of the causal lymphoid cell populations, and the effector phase also determines the course of the infection in the future.

The virus is typically able to multiply in the central nervous system (CNS) due to an unbalanced mixture of lymphocyte subsets or a delay in effector cell enlistment into the tissue. This, in turn, causes severe immune-mediated tissue damage and illness. The immune system response to brain-specific antigens can either cause autosensitization to the antigen or, if it happens too late or not strongly enough, contribute to a disastrous outcome by distributing epitopes to the antigen-presenting system in peripheral lymphoid tissue. This could be the initial trigger for subsequent autosensitised CD4+ T cell booster responses, which lead to the inflammatory autoimmune reaction known as multiple sclerosis in humans. However, a prompt and concentrated local response in the brain tissue will successfully halt the virus's growth, resulting in an infection termination mediated by the immune system that is subclinical. After virus-infected cells are removed, the local reaction will probably go down because of either self-elimination of the responsible T cell populations or through signal routes that have not yet been discovered. Much of this is highly speculative, so more data must be obtained before drawing any strong conclusions. To avoid being eliminated by T cells, viruses have developed a variety of strategies, including "hiding" in cells that do not express MHC class I or interfering

with the host cell's MHC class I presentation pathway. This may result in the virus becoming permanently embedded in the brain, a state that is almost certainly actively controlled by T cells. On the other hand, viral replication reactivation can fatal risk to the host.

Classification of Virus

Based on shared traits, viruses are grouped at different hierarchical levels of order, family, subfamily, genus, and species. Currently, there are over 30,000 different virions categorized into 71 families, 164 genera, and over 3,600 species. The morphology of viruses determines their families. Members of a virus family may only reproduce in plants, microorganisms, invertebrates, or vertebrates. Certain viral families have members that reproduce in several hosts. Apart from the physical attributes, the classification is affected by the nucleic acid pattern (ss or ds, linear or circular), the genome's segmentation or uncluttering, and the sense or antisense of the ss RNA strand. The main morphologic and chemical feature of the virus families that infect humans is the position of viral capsid assembly, and for enveloped viruses, the point of nucleocapsid envelopment, is also considered during classification.

Latinized names ending in -virus for viral genera and -viridae for virus families are now often used. Names in subfamilies end in (-virinae). Even among viruses in the same genus, they are still called by their common names. In this work, Latinized family and subfamily ends are not used frequently. It demonstrates how viruses that are significant to medicine are currently classified. [7]

Present Categorization of Important Virus Groups with Medical Importance

In the early days of virology, viruses were named after the people who discovered them and often also for shared harmful traits like organ tropism or modes of transmission. In the decades between the early 1950s and the mid-1960s, when a large number of new viruses were discovered, sigla—acronyms made up of one or more letters—were frequently used to name viruses. The names Picornaviridae and Reoviridae, respectively, are derived from pico (small) and RNA; retrovirus is derived from reverse transcriptase;

papilloma, polyoma, and vacuolating agent. Simian virus 40 [SV40]) is the source of papaviridae. This is because the agents originated in both respiratory and enteric specimens and had no relationship to newly classified viruses.

Hepadnaviridae replicates in hepatocytes by using DNA genomes, just like the hepatitis B virus does. The hepatitis A virus is currently found in the family Picornaviridae, genus Hepatovirus. The existing nomenclature guidelines specify that the siglum must have meaning for field workers and be approved by global learning groups, but they do not prohibit the creation of new sigla.

The following is the etymology of the names of the other virus families that are harmful to humans: The family Adenoviridae which was named as adeno, "gland"; named for the adenoid tissue where the viruses were discovered; Astroviridae (from the Greek for "star"); The name Arenaviridae, which means "sand," refers to the virion's sandy appearance. Bunyaviridae (named after the African location from which that stain was isolated, Bunyamwera); The term refers to calicivirus (denoted by cup or globet), which is named after the cup-shaped depressions on the viral surfaces; The term corona often describes the appearance of the peplomers that protrude from the viral surface; The name "filoviridae," which comes from the Latin filum, which means "thread" or "filament," refers to the shape of these viruses. The term "creeping herpes" (herpesviridae) characterizes the type of lesions; the family Orthomyxoviridae (ortho, meaning "true," plus myxo, meaning "mucus," a material the viruses are attracted to; The word paramyxoviridae means "closely resembling," and the word myxo Parvoviridae (from the word "small" "parvus"); Poxviridae, from the word "pustule" (pock); Togaviridae (toga, "cloak") refers to the tightly wound viral envelope, while Rhabdoviridae describes the rod shape of the viruses.

Numerous viruses with significant medical implications are still unclassified. Certain strains are difficult to grow in typical lab host systems, so they can't be obtained in large enough quantities to allow for more accurate characterization. The calicivirus family currently includes the Norwalk virus, the hepatitis E virus, and other similar agents that cause nonbacterial gastroenteritis in humans.

Non-soluble amyloid fibrils accumulate in the central nervous systems of both humans and animals, leading to potentially fatal communicable dementias such as kuru, Creutzfeldt-Jakob disease, transmissible mink encephalopathy, scrapie in sheep and goats, and Gerstmann-Straussler-Scheinker syndrome in humans.

The agents causing transmissible subacute spongiform encephalopathies have been linked to viroids or virinos, plant pathogens consisting of naked but incredibly stable circular RNA molecules ranging in size from 3 to 400 bases, or infectious genomes encased in a host cell coat, due to their resistance to chemical and physical agents. A different idea states that the term "prion" has been used to describe to a critical non-viral infectious agent for these fatal encephalopathies.

Proteinaceous agents that replicate themselves without a detectable nucleic acid are known as prions. A pathognomonic accumulation of amyloid fibers and plaques is caused by distinct mutations that cause to be a primary soluble glycoprotein insoluble, accounting for a portion of the transmissible amyloidoses that exhibit a recognizable prototype. Research on the pathogenesis of sporadic amyloidoses remains extremely ambitious, though.

A virus's size, shape, chemical composition, replication mechanism, and genome structure are all taken into consideration when classifying them. Many filamentous and pleomorphic viruses have helical-shaped nucleocapsids. Helical nucleocapsids are composed of a helical array of capsid proteins (protomers) surrounding a helical filament of nucleic acid. The nucleocapsids of many "spherical" viruses have an isosahedral shape. The number and arrangement of the capsomeres, or morphologic subunits of the icosahedron, are significant for identification and categorization purposes. Many viruses also have an outer envelope.

Chemical Composition and Mode of Replication: A virus's genome can be made up of either linear or circular DNA or RNA, which can be single- or double-stranded (ss or ds). A multipartite genome is made up of multiple nucleic acid segments, whereas a monopartite genome is made up of just

one nucleic acid molecule. Different replication strategies are required for the various types of genomes.

Structure and Function

Viruses are defined as small, obligatory intracellular parasites with an RNA or DNA genome protected by a virus-coded protein sheath. Viruses are essentially genetic elements on the move that most likely originated in cells and have a long history of coevolving with their host. Viruses need particular host cells that supply the complex metabolic and biosynthetic machinery found in prokaryotic or eukaryotic cells in order to proliferate. A full virus particle is called a virion.

The virion's main function is to transfer its DNA or RNA genome into the host cell so that the host cell can express (transcribe and translate) its genome. The viral DNA and often related basic proteins are contained in a symmetric protein capsid. The genome and the nucleoprotein, a protein connected to nucleic acids, make up the nucleocapsid. The nucleocapsid of enveloped viruses is enclosed by an outer layer of virus envelope glycoproteins studded with a lipid bilayer produced from the modified host cell membrane. [8]

Viruses are not active outside of their host cell. Certain viruses, including the poliovirus and tobacco mosaic virus, can even form crystals. Viruses are unable to generate energy. Being mandatory intracellular parasites, their ability to reproduce is entirely reliant on the complex biochemical apparatus of prokaryotic or eukaryotic cells. For the host cell to express the virus (transcribe and translate it), the virus's main objective is to insert its genome into the host cell.

An infectious virus that has completed its assembly is called a virion. Nucleic acid (single- or double-stranded RNA or DNA) and a protein coat known as the capsid, which binds to particular receptors on the virus during infection and functions as a shell to protect the viral genome from nucleases, make up basic virions. The capsid proteins are encoded in the viral genome. Because of its short size, the genome (aside from non-structural regulatory proteins required in virus replication) only codes for a minimal number of structural proteins. Capsids form as single or double protein shells and are

composed of one or more structural protein species. Therefore, several copies of the protein must self-assemble to produce the stable three-dimensional capsid structure.

The two main patterns of virus capsid self-assembly are helical symmetry, in which the protein subunits and nucleic acid are arranged in a helix, and icosahedral symmetry, in which the protein subunits aggregate into a symmetric shell that covers the nucleic acid-containing core. [7]

Important physical and chemical characteristics of the animal viruses that cause diseases in humans

Certain virus families include an additional layer called the envelope, which is usually partially produced from modified host cell membranes. Viral envelopes consist of a lipid bilayer that encloses a shell of membrane-associated proteins that are encoded with the virus. Virus-coded glycosylated (trans-) membrane proteins are studded on the outside of the bilayer. Consequently, a ring of glycoprotein spikes or knobs known as a peplomer is commonly observed on enveloped viruses.

When a virus acquires its envelope by budding through the plasma membrane or another intracellular cell membrane, the lipid makeup of the viral envelope closely reflects that of the particular host membrane. The glycosylated outer capsid and envelope proteins of viruses dictate the host range and antigenic composition of the virion. Certain host cell proteins are also crucial components of the viral envelope that budding viruses carry in addition to virus-specific envelope proteins.

Virus envelopes can be thought of as an extra layer of defence. Bigger viruses frequently have an intricate structure made up of isometric and helical symmetries that are limited to certain structural elements. Larger complex viruses, such as those belonging to the herpes or retrovirus families, are far less resistant than small viruses, such as the hepatitis B virus or members of the picornavirus or parvovirus families. [7]

Symmetry of Virus

Helical Symmetry

Similar protein subunits, or protomers, self-arrange into a helical array around the nucleic acid in the duration of replication, viruses possessing helical symmetry, with the spiral path resembling that of a spiral. These nucleocapsids can form flexible filaments or stiff, highly elongated rods; in either case, electron microscopy is frequently used to determine the specifics of the capsid structure. Helical nucleocapsids are classified as flexible or rigid, naked or enveloped, and have specific characteristics such as length, width, pitch of the helix, and number of protomers per helical turn. Tobacco mosaic virus is the helical virus that has been deliberated the most. Using x-ray diffraction studies, numerous significant structural characteristics of this plant virus have been identified. Displays the Sendai virus, a paramyxovirus family member, that is enveloped and has helical nucleocapsid symmetry.

The helical rod structure is present in the stiff tobacco mosaic virus and it represents about 5% of the virion's length. Separate 17,400-Da protein subunits, or protomers, come together to form a helix with a 6.9-nm axial repeat (49 subunits every three turns). Segments of the paramyxovirus Sendai virus's flexible helical nucleocapsids (NC) can be observed either inside the envelope (E) that protects it or outside of it once the envelope ruptures. About 1,000 nm long and 17 nm in diameter make up the intact nucleocapsid; its pitch

Icosahedral Symmetry

A polyhedron with12 vertices and 20 equilateral triangular faces is called an icosahedron. Every structural feature of the polyhedron repeats 5 times during each 360° rotation about any of the fivefold axes, which are defined by lines passing through opposing vertices. Threefold rotational symmetry axes are formed by lines through the centers of opposing triangular faces, while twofold rotational symmetry axes are formed by lines through the midpoints of opposing edges. 532 symmetry is characterized by an icosaheron (polyhedral or spherical) with threefold, twofold, and fivefold axes of rotational symmetry.

From left to right, icosahedral models were observed on the threefold, twofold, and fivefold axes of rotational symmetry. These axes run through the centres of each figure's polyhedral (upper) and spherical (lower) forms, and they are perpendicular to the page's plane.

Viral 532 symmetry was first identified by x-ray diffraction studies and subsequently by electron microscopy using negative-staining techniques. Most icosahedral viruses are composed of structural polypeptide chains, or protomers, arranged into oligomeric clusters called capsomeres. These comprise the closed capsid shell and are easily recognized by electron microscopy stained with a negative dye. The number and arrangement of capsomeres on the icosahedral shell of these viruses allow for classification. This requires locating the nearest pair of vertex capsomeres, also known as penton, that the fivefold symmetry axes cross through and figuring out the distribution of capsomeres between them.

Electron microscopy with negative stain is handled by adenoviral infections. (A) The normal isometric shell, consisting of twenty equilateral triangular faces, is visible on the capsid. A T = 25 symmetry is observed in the arrangement of the 240 hollow hexon capsomeres, 12 pentons, and 252 capsomeres.

One of the pentons capsomeres in the viral model is given a random index of h = 0, k = 0 (origin), where h and k are the indicated axes of the slanted (60°) net of capsomeres. The net axes are lines made up of the closest packed neighbouring capsomeres. Adenoviruses also have h and k axes that align with the triangle faces' corners. Any second vertex capsomere adjacent has the indices h = 5, k = 0 (or h = 0, k = 5). The capsomere number (C), which is 252, may be found using the h and k indices and the formula C = 10(h2 + hk + k2) + 2. This symmetry and capsomere count are shared by every member of the adenovirus family.

The Structure of Virus

Except for helical nucleocapsids, very little is known about how the viral DNA is bundled or organized within the core. Small virions are simple nucleocapsids that contain one to two protein species. The larger viruses have complexed nucleic acid genomes with one or more basic proteins in

their cores. These complexes are protected from the outside by an envelope or a single- or double-layered capsid composed of several protein species.

HIV-1's two-dimensional structure relates (immune) electron microscopic observations to the molecular weights of the virus's structural (glycol) proteins and to the most recent two-letter code nomenclature for structural components.

Chemical Make-Up and Replication Method

RNA virus Genomes

Diagrams representing the 21 virus families that infect humans, demonstrating several distinguishing features such as the existence of an internal nucleic acid genome and an envelope or (double-) capsid. ± indicates dsRNA or DNA; 0, circular DNA; +, sense strand; -, antisense strand.

DsRNA viruses, such as those that belong to the reovirus family, have 10, 11, or 12 distinct genome segments that encode three major capsid proteins, three RNA replication-related enzymes, and several smaller structural proteins. A hydrogen bond forms a linear ds molecule between a complementary sense and antisense strand in each segment. These viruses have complicated replication processes; only the release of sense RNA strands from the infecting virion triggers replication. [9]

The two plus-sense ss RNA molecules are the same.

That make up the retrovirus genome are each monomer, ranging in size from 7 to 11 kb, and are noncovalently linked via a brief terminal region. Retroviruses are made up of three non-structural functional proteins (reverse transcriptase, integrase, and protease: RT, IN, and PR) designated by the gag gene, four to six non-glycosylated core proteins, and two envelope proteins encoded by the env gene. The viral ss RNA is converted into double-stranded, circular pro-viral DNA by the RT. Through the action of the viral integrase, this DNA covalently binds to the host cell's DNA, enabling the transcription of the sense strands that finally give rise to progeny retroviruses. Retroviruses exhibit structural and functional

maturation following assembly and budding. In immature virions, the structural proteins of the centre are present as a significant precursor protein shell. After being processed by the viral protease, the mature virion's proteins are rearranged to create its distinctive dense, isometric, or cone-shaped core, which gives the particle its infectious characteristics.

DNA virus Genomes

A single linear dsDNA genome makes up the majority of DNA viruses. On the other hand, the circular DNA genomes of the papovaviruses, which include the papilloma and polyoma viruses, are roughly 7.8 and 5.1 kb pairs in size. DsDNA functions as a template for self-transcription in addition to mRNA. The papovavirus capsid is composed of one or two structural proteins and five to six non-structural proteins that are involved in DNA replication, cell transformation, and virus transcription.

The parvo-, erythro-, and dependoviruses are members of the Parvovirus family, which is made up of single-stranded linear DNA with a 4-6 kb size. Two to four structural protein species, each with a unique derived form from the same gene product, are present in the virion. Adeno-associated virus (AAV), a dependovirus, can only produce progeny virions when helper viruses such as herpesvirus or adenovirus are present. As a result, it is considered to be replication defective. The smallest viruses that reproduce on their own are members of the Circovirus family, which has circular single-stranded DNA that is only 1.7 to 2.3 kb in size. The isometric capsid has a diameter of 17 nm and only contains two types of proteins.

Virus-related diseases that can be fatal include encephalitis, herpes, dengue fever, chickenpox, HIV, and Covid-19.

Today, there are a lot of synthetic medications available, such as Viral infections are treated with drugs in the antiviral medication class. Broad-spectrum antivirals combat a wide range of viruses, whereas most antivirals target specific viruses. Antibiotics (sometimes referred to as "antibacterial"), antifungals, antiparasitic drugs, and antiviral drugs based on monoclonal antibodies are all classified as "antimicrobials," which also includes antiviral drugs. Antivirals can be used to treat infections because most of them are believed to be relatively safe for the host. It's critical to distinguish

them from virucides, which aren't medications but instead destroy or deactivate virus particles that are either inside or outside the body. Certain plants, like Australian tea trees and eucalyptus, naturally make virucides.

Drug resistance specific to viruses

Antiviral resistance is characterized by decreased drug response brought on by variations in viral genotypes. Antiviral resistance limits or completely eradicates a drug's capacity to successfully fight the virus it is meant to cure. Since the problem has emerged against almost all strong and targeted antimicrobials, including antiviral drugs, it will unavoidably remain a significant barrier to antiviral therapy. The Centres for Disease Control and Prevention (CDC) advise that everyone six months of age and older have a yearly vaccination to protect against influenza A viruses (H1N1 and H3N2) and up to two influenza B viruses (depending on the immunization). The first step in guaranteeing complete protection is making sure you are fully vaccinated and up to date.

Numerous human pathologies are caused by viruses. Due to the lack of preventive vaccines and antiviral therapy, the increasing global population, travel, urbanization, and infectious outbreaks have created a serious hazard to public health. New antiviral medications can be developed using resources found in refined natural products and herbal medicines. The growth of preventive vaccines and antiviral treatments has been clarified by these natural agents. Based mostly on previous attempts to address the antiviral characteristics of plant extracts and some isolated plant natural products based on preclinical (in vitro and in vivo) studies.

Synthetic Medicines and Vaccines for Virus Control

The design and synthesis of a series of N-((3-phenyl-1-(phenylsulfonyl)-1H-pyrazol-4-yl) methyl) anilines 7a-p and 8a-l was done. These series have a structural relationship to the previously synthesized and tested (N-(1,3-diphenyl-1H-pyrazol-4-yl) methyl) anilines (1a-v). The cytotoxicity and antiviral efficacy of the novel compounds in contrast to a broad panel of RNA and DNA viruses with implications for public health were assessed in cell-based experiments. In general, the examined substances showed no signs of cytotoxicity towards the employed cell lines. When compared to

the reference inhibitors 6-azauridine and ribavirin, respectively, the majority of derivatives 7a-p shown a notable improvement in potency and selectivity as they were able to interfere with YFV and RSV replication in the micromolar range. Compounds 8a-l, which have a p-methoxy substituent on the phenylsulfonyl group, have lowered or eliminated their effectiveness against YFV and completely removed their anti-RSV action. Conversely, a number of p-methoxy Analogues had a similar (8b, 8c, 8g, and 8k) or superior (8a and 8f) effectiveness in inhibiting BVDV replication in comparison to the reference inhibitor, ribavirin. When introduced two hours after infection and maintained for up to four hours after infection, compound 7e, which was chosen for occasion of additive studies on BHK-21 cell cultures infected with YFV, produced the greatest decline of virus titer. [10]

In clinical practice, drug-induced kidney injury is a common adverse effect that frequently results in acute renal failure (ARF). In patients hospitalized to the hospital or the critical care unit, it accounts for over 2% to 15% of instances of ARF, respectively. It is challenging to pinpoint the precise incidence of nephrotoxicity brought on by antiviral medications. Renal failure is caused by antiviral medications in a number of ways. There have been reports of direct renal tubular toxicity associated with several novel drugs that have distinct effects on the kidney's epithelial cells. Together with acyclovir, these include cidofovir, adefovir dipivoxil, and tenofovir. Renal failure may also be accelerated by crystal deposition in the kidney. Acyclovir and other medications have been reported to cause crystal nephropathy. [11]

Today's world has given rise to a number of heterocycles that play important roles in vital pharmaceutical agents for humankind. The quinoline scaffold has been exposed to be relevant in a wide spectrum of biological activities among the heterocycles. Numerous medicinal compounds, including saquinavir and chloroquine, have been put on the market that include quinoline molecules and have beneficial antibacterial and anticancer properties. Because of their wide-ranging biological function, scientists from all around the world have devised a variety of synthetic techniques, including the Skraup reaction and the Combes reaction. However, there are still a number of drawbacks to synthetic techniques, such as the creation of

by-products and the need for costly metal catalysts. Thus, there are ongoing efforts to design a synthetic procedure that is both effective and affordable. Because of this, we have attempted to provide a thorough explanation of the function of quinoline derivatives as an antiviral agent in this study, as well as a description of contemporary synthetic methods produced by diverse research groups. Quinoline derivatives have been shown to be effective against a variety of viral strains, including the MERS virus, hepatitis C virus, enterovirus, herpes virus, zika virus, and human immunodeficiency virus. [12] Antiviral medications (AVD) have become increasingly popular in the past several years, and patients with compromised functions and obstacles are often prescribed these medications, which increases the possibility of side effects. Nonetheless, it is challenging to definitively attribute to these medications CNS symptoms, as they may also stem from the viral illness. [13]

The chiral cyclopentenol derivative (+)-12a has been synthesized using a straightforward and workable approach. This intermediate is crucial for the production of physiologically active carbocyclic nucleosides. On a 10 g scale, the ring-closing metathesis (RCM) reaction using Grubbs catalysts and the selective protection of the allylic hydroxyl group produced (+)-12a with an overall yield of 52% from d-ribose (4). For the synthesis of artificial five-membered ring heterocyclic carbocyclic nucleosides, the crucial intermediate (+)-12a was employed. EC50 0.4 μM for the vaccinia virus and 39 μM for the cowpox and SARSCoV (severe acute respiratory syndrome coronavirus) showed strong antiviral activity of the newly synthesized 1,2,3-triazole analogue (17c). The counterpart of 1,2,4-triazole (17a) demonstrated considerable antiviral activity (EC50 21 μM) against SARSCoV.[14] Compared with 4′-oxonucleosides, there have been significantly fewer systematic structure-activity relationship studies on carbocyclic nucleosides as antiviral and antitumour medicines. The primary cause of this is the synthetic issues with the carbasugar preparation. Nonetheless, the crucial carbasugars can now be synthesized to a preparative scale thanks to the recent discovery of the ring-closing metathesis (RCM), a potent technique for the preparation of 5-membered carbasugar via C-C bond formation. Using an RCM reaction as a crucial step, this paper outlines the asymmetric synthesis of carbasugars and

carbocyclic nucleosides. In addition, the review contains important information about the design and synthesis of new carbocyclic nucleosides. [15] The 1963 licensing of idoxuridine, an iodinated derivative of 2′-deoxyuridine (1), was crucial in the development of antiviral medications. Idoxuridine is used to treat infections caused by the retinal herpes simplex virus (HSV) by incorporating it into the viral DNA. In 1980 and 2000, respectively, its structural counterparts 2′-trifluorothymidine (trifluridine) and brivudine were licensed for the treatment of HSV infections. Although 1,43 was first iodinated to produce idoxuridine, it is currently easily produced using biocatalytic methods. Only transitory phosphorylation of the nucleoside sugar unit is allowed when pyrimidine nucleoside phosphorylase (PyNP) or thymidine phosphorylase (TP) are deprived of an extra phosphate source. This permits transglycosylation with an appropriate nucleobase. In this way, one may use one of the immobilized enzymes to convert 1 to idoxuridine, trifluridine, and brivudine. Enzyme immobilization on a large-scale matrix guarantees easy catalyst isolation, allowing for simple recycling. As an alternative, a 2′-deoxyribosyltransferase might be used to generate trifluridine. [16]

Given the critical function that deubiquitinase (DUB) enzymes play in the replication of numerous viruses, including coxsackievirus, Adenovirus, HSV-1, and SARS-CoV-2, DUB inhibition has been described as a promising new strategy for the discovery of novel antiviral drugs. A new generation of 4-(2-nitrophenoxy) benzamide derivatives was created and synthesized in this study in order to satisfy the fundamental pharmacophoric characteristics of DUB inhibitors. The created compounds were molecularly docked against the deubiquitinase enzymes of the viruses listed above. We decided to perform in vitro antiviral screening against the aforementioned viruses based on significant molecular docking results. Based on biological data, the antiviral activities were found to be very strong to strong, with IC50 values ranging from 10.22 to 44.68 μM against coxsackievirus, HSV-1, and adenovirus. The most effective compounds against Adenovirus, HSV-1, coxsackievirus, and SAR-CoV-2 were discovered to be compounds 8c, 8d, 10b, and 8a, in that order. Furthermore, the substances under investigation had CC50 values ranging from 72.93 to 120.50 μM. Ultimately, the toxicity and ADMET simulations in silico showed that the

members under test exhibited a good range of drug-like characteristics. In addition, we deduced the structure-activity relationship (SAR) of the newly created and synthesized compounds in connection to their in vitro outcomes, which could assist medicinal chemists in future optimization to get more promising antiviral candidates. [17]

A complete class of antibiotics known as sulfonamides is the source of many new pharmaceuticals. A "second wind" is currently blowing through research on the new sulfonamide synthesis because of the growing capacity of organic chemistry to synthesize these compounds as well as the investigation of their biological and medicinal applications across a broad range of biological activities. By using novel reagents and techniques, it is possible to dramatically expand the number of compounds having a sulfonamide fragment in arrangement with other relevant pharmacophore groups, such as a large class of N-containing heterocycles. The widening of the activity spectrum is the outcome of these synthetic possibilities; numerous compounds display biological activity in addition to antibacterial action. Additionally, antiviral action is noted. This work provides examples of the creation of sulfonamide compounds with antiviral properties for the purpose of developing drugs against coxsackievirus B, enteroviruses, encephalomyocarditis viruses, adenoviruses, human parainfluenza viruses, Ebola virus, Marburg virus, SARS-CoV-2, HIV, and other viruses. Viral infections have emerged as a unique global public health concern within the last three years, making the creation of novel broad-spectrum antiviral medications a crucial undertaking for synthetic organic and medicinal chemistry. Sulfonamides can serve as both the side chain substituents of a physiologically active compound and a source of nitrogen for constructing a heterocyclic core that contains nitrogen. The interaction of the substrate molecule's N-nucleophilic core with the matching sulfonyl chloride frequently results in the production of the sulfonamide group. [18]

In a short period of time, the COVID-19 epidemic has taken more than a million lives globally. Healthcare professionals and the general public are experiencing anxiety over the infections because certain antiviral medications and vaccines are unavailable. Thus, it is imperative to find and develop an efficient antiviral medication as soon as possible to treat COVID-19. For the purpose of therapeutic discovery and repurposing, targeting the major

protease (Mpro) of the causative agent, SARS-CoV-2, holds significant promise. The crystal structures of SARS-CoV-2 Mpro have been published, which has enabled in silico research to find novel inhibitors against Mpro. The current study used in silico techniques to evaluate many libraries of synthetic flavonoids and benzisothiazolinones for possible SARS-CoV-2 Mpro inhibitors. After virtual screening, the compounds that made the short list were filtered using the SwissADME modelling means to eliminate molecules that had undesirable pharmacokinetics and medicinal qualities. The drug-like compounds were then put through an iterative docking process to find the best SARS-CoV-2 Mpro binders. Ultimately, the dynamic behavior, protein-ligand complex stability, and binding affinity were assessed using molecular dynamic (MD) simulations and binding free energy calculations. This led to the identification of thioflavonol, or TF-9, as a possible Mpro inhibitor. The computational investigations further demonstrated that TF-9 binds at the catalytic dyad and interacts with preserved residues in the substrate's S1 subsite. Our in-silico research showed that synthetic flavonoid analogs, especially thioflavonols, have a considerable propensity to block the primary protease Mpro, which in turn inhibits SARS-CoV-2 reproduction. [19] Several tylophorine derivatives (PBTs) based on phenanthrene substitution with a C9 substituent were created, produced, and initially assessed for their ability to inhibit the tobacco mosaic virus (TMV). When compared to tylophorine alkaloid, these molecules can be produced more effectively and with excellent yields since they have a phenanthrene core structure. According to the results of the bioassay, some of these substances have more antiviral activity against TMV in vivo than tylophorine and brand-name Ningnanmycin. Compounds 3, 4, 9, 13, and 16 in particular have been identified as possible plant virus inhibitors. The results of this study show that phenanthrene-based tylophorine derivatives (PBTs) are a new model for antiviral research and may be used to develop innovative treatments for plant virus infections. [20]

Globally, the COVID-19 pandemic caused previously unheard-of rises in illness, mortality, economic upheaval, and social unrest. SARS-CoV-2, the virus that started the pandemic, is just one of many viruses endangering public health, though. Thus, it's critical to have efficient strategies for stopping the spread of viruses and lessening their disastrous impacts on both

human and animal health. Even though there are already a lot of antivirals on the market, their effectiveness is frequently restricted due to issues like poor solubility, low permeability, poor bioavailability, untargeted release, unfavorable side effects, and antiviral resistance. By building sophisticated antiviral delivery systems on the foundations of nanotechnology, many of these issues can be resolved. Antivirals are placed into nanoparticles, which can be made of natural or manmade materials, to form these delivery systems. However, there is a growing due to health and environmental concerns, there is a focus on the progress of antiviral delivery systems using natural materials such lipids, phospholipids, surfactants, proteins, and polysaccharides. Antivirals can be handled, stabilized, and more potently by adjusting the composition, shape, size, and interfacial properties of nanoparticles. The main kinds of antivirals are described in this book, along with the difficulties that now limit their effectiveness. [21]

The antiviral efficacy of a number of newly synthesized substituted 2-pyrimidylbenzothiazoles that either included sulfonamide moieties or the amino group at the pyrimidine ring's C2 was assessed. Using Michael addition methods, guanidine or N-arylsulfonated guanidine was reacted with various ylidene benzothiazole derivatives to create the new ring system. Plaque reduction assay was used to test the newly synthesized compounds' antiviral activity against HSV-1, CBV4, HAV HM 175, HCVcc genotype 4 viruses, and HAdV7. Regarding HSV-1, it was shown that five of the twenty-one synthesized compounds demonstrated better viral reduction in the seventy to ninety percent range with substantial IC50, CC50, and SI values when compared to acyclovir. Regarding CBV4, nine substances. Seven of these synthesised 5′-O-d- and l-amino acid derivatives as well as 5′-O-(d- and l-amino acid methyl ester phosphoramidate) derivatives of vidarabine (ara-A) were shown to have comparable outcomes when produced as vidarabine prodrugs. Certain substances had comparable or greater efficacy than vidarabine in vitro in opposition to two pox viruses, and their absorption by cultured cells was enhanced in comparison to the original medication.

Models for screening of antiviral activity

MTT assay

This assay is useful in evaluating antiviral activity

For instance, the MTT test was used to assess the cytotoxicity of eighteen Bignoniaceae species in Vero cells as well as their antiviral activity against the human herpes virus type 1. [22]

Molecular docking

The world health pandemic caused by the novel coronavirus, COVID-19, which is caused by SARS-CoV-2, began in December 2019. Due to its crucial function in digesting the polyproteins transcribed from the viral RNA, the primary protease Mpro is an effective target for drugs against coronaviruses. Using computational modelling techniques, the bioactivity of a few chosen heterocyclic medications, including Favipiravir (1), Amodiaquine (2), 2′-Fluoro-2′-deoxycytidine (3), and Ribavirin (4), was assessed as COVID-19 inhibitors and nucleotide analogues in this work. The current drugs' thermal parameters, dipole moment, polarizability, and molecular electrostatic potential were estimated using density functional theory (DFT) calculations. In addition, the drugs' Mulliken atomic charges and chemical reactivity descriptors were examined. The medicines that were shortlisted were docked on the major protease of SARS-CoV-2 (PDB: 6LU7) in order to assess their binding affinity. Additionally, according to DFT calculations and docking simulation studies, amodiaquine (2) has the lowest binding energy (−7.77 Kcal/mol) and may be a good SARS-CoV-2 inhibitor, comparable to approved drugs like hydroxychloroquine and remdesivir, which have binding affinities of −6.06 and −4.96 Kcal/mol, respectively. The presence of three hydrogen bonds and other hydrophobic interactions between the medication and the essential amino acid residues of the receptor were credited with the high binding affinity of 2. Lastly, the molecular docking results were illustrated using the estimated molecule electrostatic potential data obtained from DFT. According to the DFT calculations, medication 2 has electrostatic potential. Each of these variables may contribute to the binding affinity of these medications with the active protein++ to varying degrees.

Summary: This chapter discuss about entity virus, their origin, interaction with host cells, classification, symmetry and mode of transmission specially in the CNS. It also discusses about herbs having viricidal activities.

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CHAPTER 2

HERBAL TREATMENTS FOR SEXUALLY TRANSMITTED DISEASES

DR. PRASHANT UPADHYAY

Acquired immune deficiency Syndrome

The transfer of HIV from one individual to another is known as transmission. The human immunodeficiency virus, or HIV, is the name given to the virus that causes HIV infection. The abbreviation "HIV" can be used to refer to either the virus or HIV infection.

Acquired immunodeficiency syndrome is known as AIDS. This is the most severe form of HIV infection. HIV attacks and destroys the immune system's anti-infection CD4 cells, also known as CD4 T lymphocytes. When CD4 cells are gone, the body has a harder time-fighting infections and various forms of cancer. Without therapy, HIV can gradually erode immune function, and HIV infection leads to AIDS.[1]

It is transmitted through these bodily fluids:

1) Blood - in case of blood transfusion and re-use of injection needle
2) Semen - Sexual contact with an infected person
3) Pre-seminal liquid - Sexual intercourse
4) Vaginal secretions - Sexual intercourse
5) Rectal secretions – By Anal Sex
6) Breast milk – Breastfeeding

HIV can only be transmitted by direct physical contact with an infected person. In the US, anal or vaginal sex with an HIV-positive individual

without the use of a condom or HIV prevention/treatment drugs is the main way that HIV is spread.

When injecting drugs, sharing syringes or needles with an HIV-positive person, HIV can spread from an HIV-positive woman to her child during pregnancy, childbirth, or breastfeeding. Some blood-sucking insects like ticks and mosquitoes are known as perinatal transmission of HIV. To further clarify, embracing or shaking hands with someone who is HIV-positive does not spread the infection. Furthermore, you cannot get HIV by touching objects used by an HIV-positive individual, like dishes, doorknobs, or toilet seats. [2]

Anti-HIV activity

The virus known as HIV, or human immunodeficiency, is the reason for AIDS, or acquired immune deficiency syndrome. Immunity-boosting drugs and antiviral drugs can treat this potentially fatal illness. Some extracts are helpful in the treatment of AIDS. [3]

Example 1: Rosemary

The peroxidation of phospholipid liposomes was inhibited by the extracts of rosemary and spice cocktail, with 50% inhibition concentration values of 0.0009% (v/v) and 0.0035% (v/v), respectively. The trichloromethyl peroxyl radical was reacted with rosemary extract and spice cocktail extract (at 0.2%, v/v) at estimated rates of 1.5 × 103s−1 and 2.7 × 104s−1, respectively. In the Rancimat test, both extracts exhibit strong antioxidant activity, particularly in lard. **Carnosol** and **carnosic acid**, the primary active ingredients in the herbal preparations, react at 0.05% (v/v) with rate constants of 1-3 × 106 M−1sec−1 and 2.7 × 107M−1 sec−1, respectively. The antioxidant qualities of the two herbal preparations may help them in the food matrix. The effectiveness of traditional herbal medicine, which traditional healers frequently use to treat HIV-positive patients, was investigated in an African study. After 4 to 8 months of therapy, patients showed significant improvements in their physical appearance, appetite, sense of well-being, clean skin, and urogenital swelling. They were also able to resume their job duties, gain weight, significantly decrease their viral

load, and significantly increase their immunity, as indicated by CD4 + T cell counts. [4]

Example 2: *Scutellaria baicalensis*

Scutellaria baicalensis Georgi and its identified components (i.e. baicalein and baicalin) have been shown to inhibit the infectivity and replication of HIV. Potential development of anti-AIDS compounds using molecular modeling methods will also performed in the future.[5]

Example 3: *Prunella vulgaris*

The aqueous and methanol extracts of 31 herbs traditionally used as anti-fever remedies in China were screened for their *in vitro* inhibition on human immunodeficiency virus type-1 protease (HIV-1 PR). The activity of recombinant HIV-1 protease was determined by sequence-specific cleavage at the Tyr-Pro bond of the fluorogenic substrate (Arg-Glu(EDANS)-Ser-Gln-Asn-Tyr-Pro-Ile-Val-Gln-Lys(DABCYL)-Arg) or by HPLC analysis of the cleavage products after incubation of the enzyme with a synthetic peptide substrate (Acetyl-Ser-Gln-Asn-Tyr-Pro-Val-Val-amide). Among the herbal extracts examined, the aqueous extracts of *Prunella vulgaris* and *Scutellaria baicalensis* and the methanol extracts of *Woodwardia unigemmata*, *Paeonica suffruticosa* , and *Spatholobus suberectus* elicited significant inhibition (>90%) at a concentration of 200 μg/ml.[6]

Example 4: *Woodwardia unigemmata*

The methanol extract of *Paeonia suffruticosa* still exerted potent inhibition of HIV-1 integrase (EC_{50} = 15 μg/ml) [7]

Example 5: *Paeonica suffruticosa*

The HIV was significantly inhibited (>90%) at a concentration of 200 μg/ml by the methanol extracts of *Woodwardia unigemmata, Paeonica suffruticosa*, and *Spatholobus suberect*, as well as the aqueous extracts of *Prunella vulgaris* and *Scutellaria baicalensis* [6]

Antiretroviral

A growing concern in the treatment of HIV-positive patients is antiretroviral toxicity. HIV infection is becoming a more chronic illness due to the consistent and significant decreases in opportunistic complications; as a result, more patients are using more medications for longer periods of time. In addition to more drug-specific side effects and unique clinical situations, this review concentrates on the pathophysiology, clinical characteristics, and management of the main toxicities of the 15 approved antiretroviral medications, such as lipodystrophy, hypersensitivity, and mitochondrial toxicity. Although other antiretroviral medications have been linked less frequently, the nucleotide reverse transcriptase inhibitor tenofovir and the protease inhibitor indinavir are the two most strongly linked to direct nephrotoxicity. Nephrolithiasis, obstructive nephropathy, and interstitial nephritis have been linked to indinavir, while proximal tubular dysfunction and acute kidney injury have been the main effects of tenofovir and related nucleotide analogs. There is still a wait for an herbal remedy for these illnesses.

Probiotic bacteria have been demonstrated in numerous intervention trials to be effective against HIV- and rotavirus-induced diarrhea. Despite this, probiotic bacteria's antiviral properties have not yet been thoroughly investigated. Probiotics and other lactic bacteria, together with their metabolic products, were administered in several experimental designs to non-tumorigenic porcine intestinal epithelial cells (IPEC-J2) and alveolar macrophages (3D4/2). The study employed the vesicular stomatitis virus (VSV) as a model virus. Viral inhibition and cell survival were assessed using an antiviral test, and immunofluorescence was bacteria were pre-incubated with cell monolayers. By directly attaching VSV to their surface, all of the bacteria were able to inhibit VSV binding to the cell monolayers. Other lactic bacteria and probiotics inhibited viral Hindering the adsorption and cell internalization of the VSV due to the straight trapping of the virus by the bacteria, "cross-talk" with the cells confirms the antiviral protection and the creation of metabolites with a direct antiviral effect.[8]

Herpes and its herbal cure

Important details

- Herpes simplex virus type 1 (HSV-1) infection is estimated to impact 3.7 billion people under 50 (67%) globally as the predominant cause of oral herpes.
- Herpes simplex virus type 2 (HSV-2) infection is the main cause of genital herpes, affecting 491 million people worldwide between the ages of 15 and 49 (13%).
- The majority of HSV infections are asymptomatic or misdiagnosed, even though painful blisters or ulcers that may reoccur over time are indicators of the infection.
- HIV infection can become more likely to spread when HSV-2 is present.

Summary

Herpes simplex virus (HSV), commonly referred to as herpes, is a common illness that can cause painful blisters or ulcers. Skin-to-skin contact is the major way that it spreads. It is treated but not curable.

There are two types of the herpes simplex virus.

Type 1 (HSV-1) is the primary cause of oral herpes and cold sores, two prevalent illnesses that are mainly spread through oral contact. It can potentially lead to herpes genitalia. Most adults are infected with HSV-1.

Type 2 (HSV-2) is the virus that causes genital herpes, and it is spread through sexual activity. Most people either experience mild symptoms or none at all. Ulcers or blisters could hurt and might come back because of the infection. Medication can reduce symptoms, but it won't get rid of the illness. Recurrent oral or genital herpes symptoms can be distressing.

Furthermore, genital herpes can be stigmatizing and have an impact on sexual interactions. However, the majority of herpes patients—regardless of kind—learn to cope with the illness with time.

Signs and symptoms

Most people with herpes either exhibit very little or no symptoms at all. Many people can spread the virus to other people without even recognizing they are sick. Symptoms may include painful, recurring blisters or ulcers. Enlarged lymph nodes, fever, and bodily aches can all be indicators of recent infections.

An infection's first episode (or "outbreak") may have different symptoms from later episodes. Tingling, itching, or burning are often the initial symptoms to appear in the area where the sores are likely to occur.

Common symptoms of oral herpes include blisters (also called cold sores) or open sores (sometimes called ulcers) on the lips or within the mouth.

Blisters, lumps, or open sores (ulcers) surrounding the anus or genitalia are typical signs of genital herpes.

These blisters and sores are typically painful. Cracks and leaks can cause blisters to transform into crusts.

When an infection first appears, a person may have fever, body aches, headaches, a sore throat (oral herpes), and swollen lymph nodes near the infection.

People may encounter "recurrences," or recurrent breakouts, throughout time. These are usually shorter and less severe than the first epidemic.

Treatment

Medication is commonly used to treat herpes outbreaks, whether they are new or recurrent. While they can decrease the infection's length and intensity, they cannot completely eradicate it.

The greatest outcomes for recurring episodes are obtained when treatment is started within 48 hours of the onset of symptoms.

Antiviral drugs such as valacyclovir, famciclovir, and acyclovir are frequently recommended.

It is also possible to decrease the frequency of symptoms (outbreaks) by lowering the daily dosage of any of these drugs.

Treatment is usually recommended for those who frequently feel acute pain or recurring episodes, or who want to lower their risk of herpes transmission.

Among the medications used to treat pain and soreness are paracetamol (acetaminophen), naproxen, and ibuprofen. Medications that numb the afflicted area include benzocaine and lidocaine. The herpes simplex virus is a living, alternating virus that infects nerve cells. The following circumstances could make the virus active:

- A fever or another ailment
- Sun exposure
- Menstruation;
- Physical harm;
- Emotional strain;
- Surgical procedures.

For those whose oral herpes is provoked by sunlight, minimizing sun exposure and wearing sunscreen can help lower the likelihood of recurrences.

To ease the symptoms of oral herpes, people should drink cold beverages or popsicles and take over-the-counter medicines.

The following medications are available to people with genital herpes: Put on loose-fitting clothes, take over-the-counter painkillers, and spend 20 minutes in a warm, soap-free bath.

Talking to your partner about your disease, avoiding sexual activity if you are experiencing symptoms, using a condom at all times, and not exchanging items that have come into contact with an infected person. If you are pregnant, you should consult your doctor because there is a chance that your unborn child will get herpes.

Finally, it should appear very appealing that the now-maturing construct that reactivated HZ-1 best explains the intracerebral propagation of AD changes in the human brain. Certain studies have suggested a mechanism by which statins reduce the incidence of AD. [9] These herbs are found to be potent in treatment.;

Example 1: *Agrimonia pilosa*, *Pithecellobium clypearia* and *Punica granatum*

Extracts from ***Agrimonia pilosa*, *Pithecellobium clypearia*, and *Punica granatum***, showed anti-HSV-1 activity, which was possibly contributed by the polyphenolic compounds in the herbal extracts.

Similarly, in a study, it was found that extract of following herbs *Blumea laciniata, Elephantopusscaber, Laggerapterodonta, Mussaendapubescens, Schefflera octophylla* and *Scutellaria indica,* respectively, exhibited anti-RSV activity with 50% inhibition (IC_{50}) concentrations ranging from 12.5 to 32 µg/mL, and selective indices (SI) ranging from 11.2 to 40. In addition to polyphenolic compounds, other constituents present in these extracts may also contribute to their anti-RSV activity. [10]

Example 2: Essential oils from eucalyptus, tea tree, and thyme

The herb thyme (*Thymus vulgaris*) has a peculiar scent. In addition to being used as medicine, the flowers, leaves, and oil are frequently used to flavor food. Chemicals in thyme may help treat bacterial and fungal infections. It may also have antioxidant properties and aid in cough relief.

Herpes simplex virus type 1 (HSV-1) was tested *in vitro* for the antiviral activity of essential oils from eucalyptus, tea tree, and thyme, as well as their main monoterpene compounds, a-terpinene, g-terpinene, a-pinene, p-cymene, terpinen-4-ol, a-terpineol, thymol, citral, and 1,8-cineole. The monoterpenes in these essential oils inhibited HSV by roughly 80%, and these oils were able to reduce viral infectivity by over 96%.

Although the mechanism of antiviral action has been determined, the addition of essential oils and monoterpenes to host cells, either before or after HSV infection, resulted in only weak antiviral effects. However, both

essential oils and monoterpenes showed substantial anti-HSV-1 efficacy through the direct destruction of free virus particles. Each drug tested had a dose-dependent interaction with herpes virus particles that rendered the virus inactive. [11]

Example 3: Carageenan: A Polysaccharide

In a study on HeLa cells, carrageenan, a polysaccharide, demonstrated strong antiviral activity against the Type 1 Herpes Simplex virus. It was also found that while the cell continued to synthesize cellular protein, this did not affect the attachment or entry of the virus. Apart from its antilipidemic properties, carrageenan has been linked to various health benefits for humans, including immune modulation, digestion support, and antioxidant, and antiviral properties, indicating its high bioactive potential.

1. Carrageenans, which are mucopolysaccharides derived from red algae cell walls, self-assemble into helical structures known as κ- and ι-carrageenans, which result in rigid or flexible gels, respectively. λ-carrageenans are non-gelling and do not spiral. κ-Carrageenan is utilized in the immobilization of microbiological cells by growing them in the gel. If you're searching for a natural thickener substitute, natural carrageenan is a great option. This naturally occurring polysaccharide comes from seaweed and is perfect for a wide range of products because of its thickening qualities.

2. Carrageenan promotes better intestinal health.

Because of its prebiotic qualities, carrageenan aids in the growth of good bacteria in the digestive system. This can strengthen the immune system, enhance nutrient absorption, and enhance overall digestive health.

3. Carrageenan is a vegan substitute for gelatin

Carrageenan is a fantastic substitute for gelatin if you're a vegetarian or vegan. Its gelling qualities make it perfect for a variety of vegetarian products, such as vegan cheeses, gummy candies, and plant-based meat substitutes.

4. Carrageenan is effective in terms of its antiviral properties.

Carrageenan is a common biomaterial that has only recently been found to have broad-spectrum antiviral activity. Its natural polysulphate structure acts as an indiscriminate physical barrier to viruses, including coronaviruses, that have sugar molecules on their surface. Second, the negative charge it carries interferes with viruses, preventing them from spreading. It also directly kills viruses by damaging their capsule membrane, which significantly lowers the number of viruses that can reproduce.

5. Carrageenan has the potential to reduce cholesterol.

Among its many benefits, carrageenan is useful in reducing serum LDL and cholesterol as well as regulating the development of experimental atherosclerosis.

6. Carrageenan can be used to reduce blood lipids

Carrageenan has a more marked lipid-lowering effect than other dietary fibers because it not only affects cholesterol absorption but also lowers bile acids by forming a gel that adsorbs bile acids and which the body must use to synthesize bile acids, which lowers blood lipid levels.

7. Carrageenan offers benefits in the daily care sector

Carrageenan in everyday chemical industries such as detergents and cosmetics: For avoiding re-staining, carrageenan-containing detergents work better than methyl cellulose ones. Carrageenan enhances the dispersion and storage qualities of liquid detergents.

In cosmetics, carrageenan can be combined with glycerine to create emollients due to its easy skin absorption. It can be used as an emulsifier in some shampoos and emulsions to improve the stability of the emulsion and give the product a lubricated, soft feel.

Carrageenan is a crucial ingredient in toothpaste that helps with paste suspension, thickening, and shaping. The way the paste performs is directly related to the paste's quality. Carrageenan enhances the paste's thixotropy and dispersibility, in addition to having outstanding resistance to salt and enzymes.

8. Carrageenan is a sustainable component

Red algae are used to make carrageenan, which is a sustainable ingredient made from renewable resources. Furthermore, because it's biodegradable, carrageenan doesn't harm the environment. Because of this, it's a green choice for customers searching for sustainable goods. Carrageenan is an extract from seaweed that has been used for centuries in a wide range of applications due to its many health benefits.

Carrageenan Adverse Reactions Carrageenan has several advantages, but it's also a reasonably priced ingredient. This makes it a well-liked option for food producers trying to make affordable goods. It's important to keep in mind that carrageenan has drawn criticism recently due to reports that it has adverse effects and might be hazardous to human health. However, scientific research has refuted a number of these claims. Carrage is recognized by the US FDA as a safe additive for food preservation.

It is crucial to remember that there are various kinds of carrageenan and that some (like degraded carrageenan) may be more processed or contain unfavorable additives. See a healthcare provider if you have any concerns about ingesting carrageenan. Carrageenan is a versatile ingredient that offers numerous advantages.

It is a fantastic option for customers searching for a powerful and natural ingredient because of its antiviral and cholesterol-lowering qualities as well as its sustainability and environmental friendliness. Hence, you should be aware of the advantages of carrageenan the next time you see it listed as an ingredient in plant-based dairy and meat substitutes.[12]

Human papillomavirus

Human papillomavirus (HPV) is a common sexually transmitted infection (STI) that can affect the skin, genital area, and throat. It is caused by a DNA virus of Papillomaviridae family. HPV infections can be spread through vaginal, anal, or oral sex, as well as skin-to-skin contact in the genital region

Virus-like particles, or VLPs, are multiprotein aggregates that resemble the structure and organization of real native viruses but do not carry the viral

DNA. This could lead to the development of less expensive and safer vaccine candidates. Currently, a small number of prophylactic VLP-based vaccinations are being sold globally. Examples include the hepatitis B and human papillomavirus Engerix® and Cervarix® from GlaxoSmithKline, and the hepatitis B and human papillomavirus Recombivax HB® and Gardasil® from Merck and Co., Inc. Other VLP-based vaccine candidates, like the influenza virus, parvovirus, Norwalk, and other chimeric VLPs, are either in preclinical or clinical studies. Even though several of them have shown promise in preclinical testing, they are still limited to small-scale fundamental research. This article centers on the critical function of vector-like particles (VLP) technology in next-generation vaccines against emerging and common diseases. Process control, monitoring, and optimization are examined about the effects of large-scale VLP manufacturing. The primary technical obstacles, both upstream and downstream, are noted and addressed appropriately. Alongside the most recent findings from clinical trials and the latest advancements in chimeric VLP-based technology for either therapeutic or preventive vaccination, successful VLP-based vaccine blockbusters are succinctly presented. [13]

Based on the ADME screening, only two phytoconstituents, namely stigmasterol, and clicoemodin, were selected as the best inhibitors of HPV protein. MD simulation study also revealed that stigmasterol and clicoemodin were stable inside the binding pocket of 1R9W, Stigmasterol and clicoemodin can be used as a potential investigational drug to cure HPV infections.[14]

HPV-mediated diseases are common, with high morbidity and substantial mortality. Although preventive measures exist, they are still not sufficiently widely used. Conventional treatment methods all have drawbacks. This article has discussed briefly herbs that have been studied for inhibiting HPV, including one (sinecatechins) already approved by the FDA and other national regulatory agencies as a botanical agent. While more research is warranted, the results presented here suggest that a range of herbs and medicinal foods have significant potential to prevent (in the case of brassica vegetables) and treat (in the case of green tea, immunostimulant Western and Chinese herbs, including silk vine) HPV-induced disease. [15]

Conclusively, it is evident that diseases caused by sexual intimacy may be avoided by regular use of potent herbal extracts, as these are free of side effects and have the desired effect of reducing the virulence of the virus, effective in stimulating immunity. Thus, it is preferably for prevention and cure.

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CHAPTER 3

HERBAL TREATMENTS FOR RESPIRATORY VIRAL DISEASES

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Recent News: Katalin Karikó and Drew Weissman have been awarded the 2023 Nobel Prize in Physiology or Medicine for their work that made it possible to generate mRNA vaccines against COVID-19. On October 2, 2023, The Royal Swedish Academy of Science revealed the winner.[1]

The spikes on the surface of coronaviruses resemble crowns, hence their name. The coronaviruses can be divided into four major subgroups: alpha, beta, gamma, and delta.

The first human coronaviruses were identified in the mid-1960s. Humans can contract any of the following seven coronaviruses:

Normal human coronaviruses include OC43 (beta coronavirus), NL63 (alpha coronavirus), 229E (beta coronavirus), and HKU1 (beta coronavirus).

Additional coronaviruses in humans

- MERS-CoV, the beta coronavirus that causes Middle East Respiratory Syndrome (MERS)
- SARS-CoV, the beta coronavirus that causes severe acute respiratory syndrome (SARS) COVID-19, the novel coronavirus that causes corona virus disease 2019

Worldwide, human coronaviruses 229E, NL63, OC43, and HKU1 are commonly spread to humans.

Human coronaviruses can be created by animal-borne coronaviruses, which can also evolve and infect people. Three recent examples are 2019-nova, SARS-CoV, and MERS-CoV. WHO is gathering scientists and global health specialists from around the world together to accelerate research and development, establish new rules and standards, halt the coronavirus pandemic from spreading, and help provide treatment for people affected. The R&D Blueprint has been activated to accelerate the development of diagnostic tools, vaccines, and treatment plans for this novel coronavirus. To ensure equitable access to COVID-19 medical supplies, all nations must unite.

WHO COVID-19 Research Database

The World Health Organization is gathering up-to-date, multilingual, international scientific research and data regarding COVID-19. The WHO COVID-19 Research Database is updated daily (Monday through Friday) with the addition of new expert-referred scientific publications, manual searches, and searches of bibliographic databases. This database provides a comprehensive, multilingual source for the most recent studies conducted on the topic. Even if the research may not be finished, it is always being done.

The herbs found active in combating coronavirus are:

Saikosaponins

In recent years, it has been demonstrated that many phytochemicals have potent pharmacological effects. A class of oleanane derivatives known as saponins is generally present in medicinal plants like Bupleurum spp. as glucosides. For more than a thousand years, these herbs have been utilized in traditional Chinese medicine in China. Newly available research suggests that saikosaponins may have a broad range of pharmacological actions, including liver and kidney protection, antiviral, anticonvulsant, antipyretic, anticancer, and anti-inflammatory properties. The current review provides a comprehensive synopsis and analysis of the pharmacological properties of saikosaponins, supporting their potential uses as a therapeutic agent.

The results of the investigation showed that all saikosaponins had antiviral activity at doses of 0.25–25 μmol/L, with saikosaponin B2 having the highest activity, Inhibitory concentration (IC50 = 1.7 ± 0.1 μmol/L).

In recent years, it has been demonstrated that many phytochemicals have potent pharmacological effects. One kind is known as saikosaponins. It's interesting to note that neither of the saikosaponins, B2 (CC50 = 383.3 ± 0.2 μmol/L; SI = 221.9), **where CC50** denotes cytotoxic concentration 50%, nor A (50% cellular cytotoxicity (CC50) concentration = 228.1 ± 3.8 μmol/L; selectivity index (SI) = 26.6), showed any cytotoxic effects on target cells at concentrations that produced antiviral activity. When saikosaponin B2 was administered at different times pre-infection (-4 to -1 h), coinfection (0 h), and post-infection (1-4 h), time-of-addition tests revealed that it strongly inhibited human coronavirus 229E infection at 6 μmol/L. Furthermore, saikosaponin B2 showed a suppressive effect on viral attachment and penetration. The current investigation suggests that saikosaponin B2 has potent anti-corona viral action and may be effective. [2]

Lycoris radiata

It is a bulbous plant that belongs to the Amaryllidaceae family and is native to China, Japan, and South Korea. When galantamine, a representative alkaloid of Amaryllidaceae plants, including L. radiata, is present, acetylcholinesterase inhibition is selective and dominant. Despite the economic and functional relevance of L. radiata, there is a relative dearth of data on its molecular biology and biochemistry.

Scientific name: *Lycoris radiata*
Family: Amaryllidaceae
Kingdom: Plantae
Order: Asparagales
Subfamily: Amaryllidoideae

More than 200 Chinese medicinal herb extracts were investigated for their antiviral qualities against the Severe Acute Respiratory Syndrome-associated coronavirus (SARS-CoV) utilizing 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium inner salt

(MTS) test for viral cytopathic effect (CPE). The most effective of these is found to be Lycoris radiata. To identify the active component, the L. radiata extract underwent further fractionation, purification, and CPE/MTS testing. By using this method, a single chemical with an EC50 value of 15.7 ± 1.2 nM was found to be an anti-SARS-CoV component: lycorine. This chemical has a CC50 value in the cytotoxicity test of 14980.0 ± 912.0 nM and a selective index (SI) greater than 900. The results showed that four herbal extracts and lycorine are viable candidates for the development of innovative anti-SARS-CoV drugs for the

treatment of SARS. [3]

Sophora flavescens Ait. and Scutellari abaicalensis Georgi A species of plant in the Fabaceae family's genus Sophora is the shrubby sophora, also known as Sophora flavescens. This genus, which is widely dispersed throughout Asia, Oceania, and the Pacific islands, is made up of about 52 species, 19 variations, and 7 forms.

After further purification of the active extracts from Sophora flavescens Ait, Scutellaria baicalensis Georgi made it possible to identify the potent anti-RSV components as anagyrine, oxymatrine, sophoranol, wogonin, and pyroxylin A. [4]

Emodin

Emodin, an anthraquinone derivative, is found naturally in several widely used Chinese medicinal herbs, such as Rheum palmatum, Polygonum cuspidatum, and Polygonum multiflorum. Emodin has been a component of traditional Chinese medicine for almost 2,000 years and is currently included in many herbal formulations. Emodin may have a wide range of pharmacological properties, including anti-inflammatory, hepatoprotective, antioxidant, anticancer, and antibacterial activities, according to a growing body of research. However, emodin can also be toxic to the kidneys, liver, and reproductive system, particularly if used frequently and in excessive doses. Research on pharmacokinetics has demonstrated that rats' oral bioavailability of emodin is low due to its high glucuronidation. This review's objective is to offer a comprehensive summary of the pharmacology, toxicity, and pharmacokinetics of emodin that have been

previously published, with a focus on its biological characteristics and mechanisms of action. Previous research has demonstrated that the SARS coronavirus (SARS-CoV) open-reading frame 3a creates a cation-selective channel that may be produced in the infected cell and afterward plays a role in virus release. It is anticipated that medications that obstruct the ion channel that the 3a protein creates will stop viruses from releasing and may be utilized to develop novel therapeutic medicines. This work shows that emodin, with a K1/2 value of about 20μM, can block the release of the coronaviruses from HCoV-OC43 and SARS-CoV by blocking their 3a ion channel. One may argue that creating antiviral medications would be a useful use for viral ion channels in general. [5]

Tea

Tea is the most affordable beverage that people consume, followed by water. Tea drinking has been linked to health advantages since ancient times. This idea is being supported by a strong body of scientific study in medicine. The volume of research supporting tea drinking's positive health effects grows with every new study that is released in the scientific literature. The tea plant *Camellia sinensis* has been cultivated for millennia, and its leaves have been utilized for therapeutic purposes. Tea is a popular beverage all over the world, and some of its ingredients are now being found to have medicinal benefits. Studies showing green tea's anti-cancer effects in humans, animals, and cell cultures have produced encouraging results. There is mounting evidence that black tea could provide similar health advantages in several crippling illnesses that affect people, including maintaining metabolic and cardiovascular health. Numerous research findings indicate that the polyphenolic compounds found in both green and black tea may have advantageous effects in preventing cardiovascular diseases, specifically atherosclerosis and coronary heart disease. Tea consumption is also linked to numerous health benefits, including anti-aging. There is growing evidence that the majority of the physiological effects of tea are attributed to the main polyphenolic compounds found in black and green tea, respectively, catechins and theaflavins. There is evidence from clinical and epidemiological studies that tea consumption is associated with general health promotion and the prevention of chronic diseases like cancer and cardiovascular diseases.

SARS-CoV is the virus that causes SARS, or severe acute respiratory syndrome. The virus-encoded 3C-like protease (3CLPro) is thought to be necessary for the replication of SARS-CoV in infected host cells. In this study, 720 substances from a library of natural products were evaluated for their ability to inhibit 3CLPro. The two chemicals in the library that were found to be inhibitory were tannic acid (IC50 = 3 μM) and 3-isotheaflavin-3-gallate (TF2B) (IC50 = 7 μM).

These two compounds belong to a class of organic polyphenols found in tea. Further investigation was done on the 3CLPro-inhibitory activity of extracts from a range of tea varietals, including black, green, oolong, and pure tea. Results of the study indicated that extracts from pure and black teas inhibited 3CLPro more potently than extracts from green or oolong teas. The capacity of several additional well-known tea blends to inhibit 3CLPro was also evaluated. The results of the investigation showed that caffeine, (-)-epigallocatechin gallate (EGCg), epicatechin (EC), theophylline (TP), catechin (C), epicatechin gallate (ECG), and epigallocatechin (EGC) did not suppress 3CLPro activity. Theaflavin-3,3′-gallate (TF3) was shown to be the sole compound that inhibited 3CLPro. The results of this investigation have led to the identification of novel, potent 3CLPro inhibitors. [6]

The infection was caused by a new coronavirus that surfaced in 2019 called SARS-CoV-2. The human respiratory system is the primary organ affected by the pathogenic virus COVID-19, while it can also affect other organs. Although previous beta coronavirus strain outbreaks have been documented, including the 2012 outbreak of Middle East respiratory disease (MERS-CoV) and the 2002–2003 outbreak of severe acute respiratory syndrome SARS-CoV1, SARS-CoV-2 is a new strain that has not yet been linked to any human infections. The aforementioned infections are extremely dangerous for global economies and public health. Although there is currently no recognized treatment for SARS-CoV-2 infection, some drugs seem to be useful in blocking the virus that causes the illness. Previous research has shown that natural substances like herbs and mushrooms have strong antiviral and anti-inflammatory properties. Thus, natural compounds may have a promising future as COVID-19 treatments. The following herbs are found to be potent:

Inonotus obliquus (IO)

The chaga mushroom, or Inonotus obliquus (IO), may provide some protection against the SARS-CoV-2 virus. IO is a widely used raw material that is commonly farmed in Asia, Europe, and North America for a variety of medical problems. We have analyzed the top herbs and mushrooms in this review based on evaluations of their antiviral and anti-inflammatory qualities conducted in laboratories.[7]

With the start of the new decade, modern human societies have been severely impacted by the COVID-19 epidemic. The COVID-19 causal agent, SARS-CoV-2, is mutating and recirculating into new strains. Three novel antiviral peptides (AVPs) against SARS-CoV-2 have been discovered here. These AVPs are comparable to the SARS-CoV-2 spike glycoprotein. Seq12, Seq12m, and Seq13m are examples of antiviral peptides that can disrupt the SARS-CoV-2 receptor-binding domain (RBD), which is required for interaction with the angiotensin-converting enzyme 2 (ACE2). Furthermore, these AVPs maintain their antiviral characteristics even after 25 mutations (based on FoldX and Rosetta) are inserted into the RBD. Additionally, Seq12 and Seq12m exhibited very little cytotoxicity. Additionally, the binding free energies determined by the MM-PB/GBSA technique accord with the results of the molecular docking experiments. AVPs and the viral membrane protein (M) exhibited favorable molecular interactions, which may indicate that AVPs can prevent the virus from re-packaging. This study concludes that Seq12, Seq12m, and Seq13m may be useful in the fight against SARS-CoV-2. In the future, these AVPs may also help with SARS-CoV-2 nasal spray and virus detection.[8]

SARS and its herbal cure

The virus that causes severe acute respiratory syndrome (SARS) is a coronavirus. It was initially identified at the end of February 2003, during an outbreak that began in China and spread to four other countries. The World Health Organization (WHO) coordinated the global investigation and worked closely with the health authorities in the affected countries to provide epidemiological, clinical, and logistical support to contain the

outbreak. The Global Outbreak Alert and Response Network (GOARN) enabled this collaboration.

With the aid of the Global Outbreak Alert and Response Network (GOARN), WHO oversaw the global investigation and collaborated closely with the health authorities in the impacted nations to provide epidemiological, clinical, and logistical support to contain the outbreak.

Like the cold and influenza, SARS is an airborne virus that can spread through tiny salivary droplets. It was the first serious and easily spread disease of the twenty-first century, and it was evident that it could spread through international flight lanes.

Additionally, surfaces that have been touched by an infected person can indirectly spread the SARS virus.

Most SARS patients were previously healthy adults in the 25–70 age range. There have been a few young people under the age of fifteen who may have contracted SARS. The current WHO case definition for probable and suspected SARS cases states that 3% of patients with these illnesses often pass away from their conditions.

According to WHO recommendations, each country should set up a reference laboratory to examine and/or refer specimens from possible SARS cases. National reference laboratories are welcome to send isolates and specimens to members of the WHO multicentre collaborative network once appropriate contact and shipment arrangements have been arranged. Labs using SARS-specific PCR tests should put quality control procedures in place and/or locate a partner lab within their country or among the WHO-collaborating research labs to confirm their positive results.

Labs performing SARS-specific PCR tests should use strict standards to validate positive results, especially in low-prevalence locations where the positive predictive value can be lower: The right controls should be used in each PCR run to ensure the desired results. To identify PCR inhibitory chemicals (inhibition control), the patient sample should be spiked with a weak positive control; one negative control for the extraction process; one water control for the PCR run; one positive control for the extraction and

PCR run; Should a positive PCR result be obtained, it should be verified either by testing the same sample in a different laboratory OR by repeating the PCR using the original sample.

Test specificity will rise when a second genome region is amplified.

The WHO collaborative multicenter research project on SARS diagnosis has made a test kit with positive and negative controls available.

Communicable Diseases

A potentially fatal type of pneumonia called severe acute respiratory syndrome (SARS) is brought on by the SARS coronavirus (SARS-CoV). It infected over 8000 people globally between late 2002 and mid-2003, with the majority of cases occurring in China due to the lack of effective Western medications. These herbs are effective when used as medicine.

***Houttuynia cordata* Thunb. (Saururaceae)**

In traditional Chinese medicine, *Houttuynia cordata* was used to treat SARS and other disorders, even by Chinese scientists. However, as of 2018, there is no high-quality clinical research to support the safety or efficacy of these uses. When *H. cordata* is injected, it can result in extremely serious allergic reactions.[9]

Family: Saururaceae
Scientific name: Houttuynia cordata
Kingdom: Plantae
Order: Piperales

Chinese scientists shortlisted *Houttuynia cordata* to treat SARS since it is commonly used to treat pneumonia. It was discovered that HC raised the percentage of T cells that were CD4+ and CD8+. Moreover, it caused a significant increase in the amount of IL-2 and IL-10 released by mouse splenic cells. In terms of the antiviral component, HC showed a significant reduction of SARS-CoV 3C-like protease (3CLpro) and RNA-dependent RNA polymerase (RdRp). On the other hand, an oral acute toxicity test showed that laboratory rats did not exhibit toxicity from HC when given orally at a level of 16 g/kg.

Isatin derivatives

A variety of isatin compounds were synthesized and assessed with SARS CoV 3C-like protease present. N-1 and C-5 alterations were examined in order to elucidate the differences between the substrate binding sites of the SARS CoV 3C-like protease and the rhinovirus 3C protease. Compound Sf has an IC50 of 0.37 μM and shows substantial suppression. Subsequent analysis showed that, in contrast to isatin derivatives' irreversible covalent binding to human rhinovirus 3C protease, all of the compounds investigated in this study are noncovalent reversible inhibitors.[10]

Influenza and its Herbal Cure

Anti-influenza activity is shown by two species *Bergenia ligulate* and *Nerium indicum*. Its 50% inhibitory dose is 10 μg/ml. Both of these extracts are found active in treatment;

a) *Bergenia ligulata* and *Nerium indicum*

Two species, *Bergenia ligulata* , and *Nerium indicum* showed the maximum anti-influenza viral activity with a 50% inhibitory dose. *Holoptelian integrifolia* and *N. indicum* exhibited considerable antiviral activity against herpes simplex virus. None of these extracts exhibited cytotoxic effects. Additionally for *B. ligulata* and *H. integrifolia* partial protease inhibitory activity was estimated.[11]

b) Antiwei

Mahuang (*Herba Ephedra*), Baimaogeng (*Rhizoma Imperatae*), Gagmen (*Radix puerariae*), Guizhi (*Ramulus Cinnamoumum*), Kuxingren (*Semen Armeniacae amarum.*), Ganjiang (*Rhizoma Zingiberis*) and Gancao (*Radix Glycyrrhizae*).

Compared to placebo, antiwei improved patient recovery by 17% ($P < 0.001$) and decreased the severity of illness by 50% ($P < 0.001$) in both the influenza-like and influenza-confirmed populations, as shown by the median symptom score. After receiving Antiwei for one day, as opposed to a placebo, the influenza-confirmed patients reported decreased fever (P =

0.002), cough (P = 0.023), and expectoration (P = 0.004). The profiles of adverse events were comparable between Antiwei and placebo. [12]

c) QinxiangQingjie

Huang qin (*Radix scutellariae*), Guang huoxiang (Patchouli), Chan tui (*Periostracum cicadae*), Shi gao (*Gypsum fibrosum*), Ge gen (Kudzu Root), Da huang (*Radix et RhizomaRhei*), Chi shao (*Radix Paeoniae Rubra*), Ban lan gen (*Radix isatidis*), Jie geng (*Radix platycodi*), Xuan shen (*Radix scrophulariae*), Shan dou gen (*Sophora subprostrata*), and Gan cao (*Radix glycyrrhizae*) make up the traditional Chinese herb preparation Qinxiang Qingjie (QXQJ).

A total of 231 kids were randomly assigned to accept either oseltamivir (n=114) or QXQJ (n=117) in research. According to the Full analyst set, FAS, and Per protocol set, PPS data, the median clinical recovery period for both groups was three days (P>0.05). For both groups, the median time to defervescence was 36 hours for PPS and FAS (P>0.05), and there was no difference between the two groups for the remaining secondary endpoints (P>0.05). At least one adverse event was recorded by 14 patients (12.39%) in the QXQJ group and 14 patients (12.50%) in the oseltamivir group, respectively. There was one significant adverse event in the QXQJ group. The frequency of adverse events or adverse medication responses did not significantly differ between the groups. [13]

d) Ginseng, Salviae

In a mouse model of influenza virus infection, we have examined the adjuvant functions of widely used herbal medicines (ginseng, Salviae) and their impacts on early immune responses. Compared to immunization with PR8 alone, intranasal co-administration of inactivated influenza virus A (PR8) and ginseng or Salviae extract boosted the levels of influenza virus-specific antibodies and neutralizing activity and provided protective immunity. Salviae co-administration considerably boosted IFN-γ and IL-2 cytokine releasing splenocytes whereas ginseng caused high amounts of IL-4 and IL-5 cytokine releasing cells after challenge infection. During challenge virus infection, the lungs of naïve mice had significantly higher amounts of pro-inflammatory cytokine IL-6 and early activation marker

CD69-expressing cells, which could potentially represent a mechanism in lung inflammation that resulted in death. Conversely, after receiving ginseng or Salviae in addition to their vaccination, the immunized mice exhibited a large increase in IgA antibodies specific to the influenza virus in their lungs following challenge virus infection, did not release IL-6, and regulated CD69 expressing immune cells. Thus, these findings suggest that Salviae and ginseng function as immuno-modulators throughout influenza virus infection as well as mucosal adjuvants against influenza virus. [14]

e) *Cinnamomum cassia*

Kakkon-to, a blend of seven traditional herbs, demonstrated unprecedented antipyretic efficacy in a mouse intranasal influenza virus infection model by inhibiting the synthesis of interleukin-1α in response to interferon. This methodology was used to characterize antipyretic chemicals from the herbs that have such new biological actions. Among the plants, *Cinnamomum cassia's* fractions that could be extracted using an organic solvent exhibited antipyretic properties. Out of 48 cinnamyl derivatives and related chemicals that might be primarily implicated in fractionation, we chose six antipyretic drugs. The regulating activity of interleukin-1α was substantially linked with their antipyretic activity. In mice treated with interleukin-1α, four of them demonstrated a distinct antipyretic effect mechanism from aspirin and reduced interleukin-1α production to a basal level. The link between the four compounds' structures and bioactivities revealed that an ester bond was crucial for the regulation of interleukin-1α and antipyretic effects. By inhibiting interferon-induced interleukin-1α production, these drugs may be helpful in studying the role of interleukin-1α-producing cells in fever generation and the process of effervescence. [15]

f) *Lonicera japonica* and *Fructus forsythiae*

One of the main challenges for current research is understanding how the many chemical components of medicinal herbs contribute to the overall pharmacological impact. Furthermore, several components have two or even three roles in the battle against the influenza virus, which adds another level of complexity to studies on pharmaceuticals. Here, we presented a brand-new systems pharmacology model that combines network analysis,

targeting, and pharmacokinetic screening. By employing this model, two notable herbs Lonicera japonica and Fructus forsythiae were investigated for their pharmacological influence on influenza, inflammation, and other disorders. One noteworthy pharmacological feature of these chemical components in both herbs is their Janus function, which directly inhibits virus replication while concurrently enhancing the host immune response [16]

g) *Andrographis paniculata* (kalmegh), *Pelargonium sidoides* (African geranium), máhuángtāng (maō-tō, ephedra decoction), and antiwei formula

Viral respiratory infections (VRI) have long been treated and prevented with herbal medications. An overview of these herbs is given here. There is extensive discussion of the advantages and consequences of a variety of antiviral herbs. Because the majority of these herbs naturally stimulate the immune system and reduce inflammation, they may assist in prevent an overreaction of the immune system (a "cytokine storm") to virtual reality illnesses while also enhancing the immune system's ability to fight off infections. There is a discussion of the scientific foundation for these claims. Sambucus nigra (black elder) fruit, *Andrographis paniculata* (kalmegh), *Pelargonium sidoides* (African geranium), máhuángtāng (maō-tō, ephedra decoction), and antiwei formula are major herbs having clinical trial evidence that they assist resolve VRI described in detail.

Reviewing the shortcomings of studies on *Echinacea angustifolia* (narrow-leaved purple coneflower), especially those that employed much too low dosages A discussion of the evidence supporting the prevention of VRI by several herbs, including *Panax ginseng* (Asian red ginseng), *Panax quinquefolius* (American ginseng), *Camellia sinensis* (green tea), and *Allium sativum* (garlic), follows the presentation of a customized method to formulation for VRI patients.

h) *Emblica officinalis* L. (EO), *Osmium sanctum* L. (OS) and *Tinosporacardifolia* (Thunb.) Miers (TC

Emblica officinalis L. (EO), *Osmium sanctum* L. (OS), and *Tinospora cardifolia* (Thunb.) Miers (TC), either alone or in combination with other

herbs, are effective in treating conditions like colds, warts, skin maladies, influenza, anemia, diabetes, lung disorders, elevated cholesterol, and as an immune-stimulating agent in cancer cases. The three natural medicines mentioned above contain abundant amounts of vital amino acids, calcium, iron, terpenoids, tannins, polyphenols, and vitamin C, among many other phytoconstituents. Using traditional herbs on a regular basis helps prevent cancer, regenerate the body, and treat age-related illnesses. Chronic illnesses like high blood pressure, diabetes, AIDS, influenza, persistent colds and coughs, persistent infections, persistent exhaustion, and persistent inflammatory problems may be fought by them. Ayurveda describes them as one of the best herbs for diabetes, bleeding disorders, strength promoter and others diseases.

Alveolar macrophages from mice exposed to electronic cigarettes had reduced phagocytosis, which contributed to the poor clearance of germs. E-cigarette exposed mice showed higher lung viral titers in response to influenza A virus infection, and increased virus-induced sickness and mortality. In conclusion, this study presents a model of E-cigarette exposure in mice and shows that E-cigarette exposure results in decreased lung anti-microbial defenses. Therefore, users of e-cigarettes who would otherwise smoke cigarettes should have their immune systems and susceptibility to bacterial and viral infections thoroughly examined. [17]

We offer a method for conceptually examining the kinetics and regularities of influenza A virus (IAV) infection in humans. In order to investigate the estimations of the "numbers" (Zinkernagel et al., 1985) describing immune responses and evolutionary established interferon in simple IAV infection, a multiparameter mathematical model that enables direct quantitative references to biological reality is developed. The mathematical model of the antiviral immune response, which was previously utilized to study acute hepatitis B virus infection (Marchuk et al., 1991a, b), has been expanded and adjusted to account for the combined response of the immune and interferon systems during interferon-associated virus infection. The main source of interferon that causes lung epithelial cells to develop antiviral resistance is thought to be macrophages that have infiltrated the epithelium of the airways. The model is designed as a delay-differential system with roughly sixty parameters that describe the speeds of several processes that

go into an IAV infection's normal course. The generation of a consistent data set that presents a broad image of simple IAV infection is a crucial component of the adjustment between the model and different data on influenza immunity. It provides a coherent theoretical explanation of how an infection normally progresses and the antiviral immune response that is appropriate for model fitting. A thorough discussion of the parameter estimates for the processes considered in the model is presented. The organization and dynamic characteristics of the processes causing IAV infection are investigated using the quantitative model. Analysis is done on the threshold condition for virus-free host immune protection against IAV infection. The kinetics of the simple IAV infection are examined, together with the respective contributions of humoral, cellular, and interferon reactions. Sensitivity studies provide a quantitative measure of the contribution of interferon, IAV-specific immune mechanisms, and parameters of virus-sensitive tissue to the variations in infection duration and severity. It has been demonstrated that differences in a virus-epithelial cell system's characteristic have a greater impact on infection severity than does the antiviral immune response. It is demonstrated that to produce immunity against the infection, the kinetics of the non-specific interferon response and the adaptive antigen-specific immune reactions must be precisely coordinated. [18]

VRI Herbs

In general, a variety of plants with various effects are required to treat VRI rather than a single herb. Herbs that directly combat invasive viruses are arguably the most significant among these. Here, the main causes of VRI—rhinovirus, metapneumovirus, coronavirus, adenovirus, parainfluenza, enterovirus, respiratory syncytial virus (RSV), and influenza viruses—will be discussed.

Evidence has been shown to support the anti-VRI properties of several of the mentioned herbs. Most of these herbs probably have very broad activity against respiratory viruses, even if their clinical efficacy is broad and those that have been examined against a wide variety of species show favorable results across most of them. The majorities of the plants listed as being antiviral in but not in have never really been tested for this property. They

are categorized as such due to their demonstrated antimicrobial activity against other species unrelated to VRI and their clinical consequences. It is interesting that no research on any of these herbs about their impact on the metapneumovirus could be located. As this is a very common cause of VRI other than attempting to match these herbs to a particular virus that a patient is infected with. This is rarely an option either, because there is still no rapid, inexpensive test to identify the virus a patient has, other than influenza. This kind of matching by infecting organism is further hampered by a lack of comprehensive study on which herbs are beneficial for infections by which organism. Instead, a variety of herbs from two or three distinct families and with various chemistries are suggested, and the antiviral plants are selected based on their secondary qualities. By doing so, antiviral synergy is maximized and resistance is prevented.

Antiviral Herbs with an Edge

Within botanical families, three specific classes of antiviral herbs are worthy of special attention. Three plants belonging to the *Apiaceae* family are clinically powerful respiratory-tract antivirals that also function as immune stimulants and inflammatory modulators. These herbs are *Liberticum* spp. (oshá, oshala), *Lomatium dissectum* (desert parsley, lomatium), and *Osmorhiza occidentalis* (western sweet cicely). For every herb, the part that is used is the root. Three notable species are used worldwide for colds and influenza, among other purposes: *Ligusticum porteri* (oshá), from the mountainous regions of the desert southwestern United States and northern Mexico; *L. grayi* (Gray's lovage), from the Pacific Northwest; and *L. striatrum* = *L. chuanxiong* (chuān xiōng). The primary active ingredients in these herbs are thought to include ligustilides, other phthalides, and furanocoumarins. Ligustilide, for example, is the only known antiviral component found in *Ligusticum* spp. Although oshá has been heavily overharvested in the wild close to cities, it is still widely distributed in the countryside. To ensure the long-term viability of this priceless plant, work on its cultivation is still ongoing.

With the exception of chun xiong, which has garnered the greatest attention and has at least been proven to be inflammation-modulating, none of these herbs have been extensively examined in the modern day. Herbs do not

function like pharmacological anti-inflammatories, which potently inhibit one key pathway, as was previously argued. Instead, they have a milder effect on a number of pathways, necessitating the use of specific terminology. This action is supported across the genus by the discovery that (Z)-ligustilide also modulates inflammation. While desert parsley, oshá, and chun xiong have fairly overpowering, repulsive flavors, western sweet Cicely has a faint licorice-like flavor that makes it quite palatable. These herbs are advised for general use due to their peculiar chemistry, potent activity, and ability to be effective at low doses. These herbs are generally highly safe, although there is a rare observed possibility that they could cause photosensitivity dermatitis.

The chemistry of the plants of the *Lamiaceae* family, particularly the monoterpenoids, is entirely different. Several other mints have antiviral and other therapeutic benefits related to VRI, including *Prunella vulgaris* (heal-all), *Thymus vulgaris* (thyme), *Rosmarinus officinalis* (rosemary), and *Salvia apiana* (white sage). Based on flavor, patients generally accept these well. In a double-blind, randomized study, thyme and Hedera helix (English ivy) leaf significantly reduced cough in comparison to placebo in 361 German individuals with severe bronchitis.[19]

The third family category of antivirals consists of trees from the *Pinaceae* and *Cupressaceae* families of evergreen plants. Resin and branch tips from *Pinus* spp. (pine), *Abies* spp. (real firs), *Picea* spp. (spruces), *Thuja* spp. (cedars), and *Juniperus* spp. (junipers) are all respiratory tract-affinity antiviral and inflammatory modulators. Due to their year-round availability and minimal impact on the trees when adequate amounts of medication are harvested, these herbs are incredibly sustainable sources of medicine.

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chun xiong have fairly overpowering, repulsive flavors, western sweet Cicely has a faint licorice-like flavor that makes it quite palatable. These herbs are advised for general use due to their peculiar chemistry, potent activity, and ability to be effective at low doses.

The significance of the antiviral herbs' ability to modulate inflammation is bolstered by research on a few of them. In an in vitro model, desert parsley has been demonstrated to reduce the production of CXCL10, a cytokine that is strongly linked to hazardous cytokine storms in severe influenza. Although this is still not well investigated, it's possible that desert parsley concurrently raises other cytokines that help to block the virus rather than cause cytokine storm. Chuān xiōng, *Glycyrrhiza uralensis* (Chinese licorice, gān cĎo), and *Forsythia suspensa* (forsythia, lián qiào) all suppressed the formation of CCL5, often referred to as RANTES, a participant in cytokine storms. It has been demonstrated that the diterpenoids found in garden sage and rosemary prevent the synthesis of certain cytokines linked to cytokine storms. Diterpenoids from rosemary and garden sage have been shown to inhibit the production of multiple cytokines associated with cytokine storms. Heal-all has repeatedly been shown to have inflammation-modulating effects. Human studies are lacking, but these results support what is seen clinically: mitigation of severity and lethality of influenza and other VRI in patients who take these herbs in sufficient doses.

Clinical Trials in Acute VRI

It has been demonstrated that a variety of the herbs covered here are useful in the treatment of VRI. Among the most well-known is the fruit of Sambucus nigra, sometimes known as black elder. In the first trial, which was double-blind, 40 adults and children in southern Israel who had been diagnosed with influenza B were randomly assigned to receive either black elderberry syrup or a placebo (1 tbsp b.i.d. for children or 2 tbsp b.i.d. for adults). When compared to the placebo group, the black elder group experienced significantly reduced levels of both symptom intensity and duration (mean 1.3 days shorter). In a comparable double-blind study, 60 adult Norwegians with influenza A or B were randomly assigned to receive a placebo or 15 mL of black elder syrup. Once more, black elder dramatically reduced the severity of symptoms as compared to placebo, and

in this instance, black elder recovery occurred four days faster on average. Additionally, compared to the placebo group, the black elder group used rescue medication much less frequently. In either of these trials, there were no negative outcomes.

In a more recent study, 312 adult Australians traveling abroad by coach were randomized to receive either a placebo or 300 mg of black elder capsules taken twice daily before, during, and after travel. Every individual took the prescribed medication for a total of fourteen days. Approximately 50% had received an influenza vaccination. Regarding the frequency of clinical VRIs, there was no variation observed among the groups. Comparing the black elder group to the placebo group, the duration and intensity of these colds were, however, noticeably shorter and lower, respectively. There was no discernible difference in the negative effects between the two groups, indicating that black elder did not pose a serious threat.

Since Josef Popp created the proprietary German formula BNO 1016 in 1933, it has been investigated quite thoroughly for VRI. The components in it are somewhat unique, except black elderflower, which is still widely used for VRI in Western herbal therapy. In vitro tests have demonstrated the mixture's effectiveness against adenovirus, rhinovirus, parainfluenza, and RSV. In rodents, it has also been shown to have anti-inflammatory properties. The dried extract is typically taken at 160 mg t.i.d.

BNO 1016 is effective in treating patients with VRI in numerous clinical trials. A total of 589 adult Germans with VRI were assigned to either BNO 1016 or placebo for 15 days in the two most recent double-blind trials. In both trials, BNO 1016 considerably lessened the severity of symptoms when compared to placebo. The formula has very few negative effects. In a second double-blind experiment, BNO 1016 considerably reduced symptoms when compared to placebo in 386 adult Germans with acute VRI. Seven were the required number to treat with BNO 1016 to have a clinically meaningful decrease in symptoms. It was a fairly safe formula once more. In a previous open study, 40 Russian children with suppurative otitis media who were receiving antibiotics, nasal decongestants, and some surgery—some of whom were also receiving BNO 1016 treatment—were examined. When compared to the non-herbal formula group, the exudate cleared much more

quickly in the former. Lastly, the mixture is also useful in the treatment of allergies, which are occasionally clinically similar to upper VRIs.

In Ayurvedic and other traditional Asian medical systems, Andrographis paniculata, also known as kalmegh, is a well-known tropical species from the Acanthaceae family that is endemic to South Asia and is used to cure VRI. It is also quite bitter, earning it the moniker "king of bitters" at times. To avoid its bad taste, it is best taken in a capsule. Seven double-blind, randomized therapeutic trials including different kalmegh formulations in patients with upper VRIs were assessed by a meta-analysis. When compared to a placebo, kalmegh considerably lessened the intensity of cold symptoms. It did so without causing any harm. A pill or encapsulated extract of kalmegh should be taken 1-3 g t.i.d.[20]

Belonging to the Geraniaceae family, *Pelargonium sidoides*, often known as African geranium, is indigenous to South Africa, namely the Eastern Cape region, which includes Lesotho. It is noteworthy that this family contains several species with antiviral properties, most notably *Geranium sanguineum*. Although the quality of the trials was generally low, a meta-analysis of 10 trials using African geranium root extracts for VRI in children and adults found evidence that they are more effective than placebo. With this herb's excellent safety profile, therapeutic usage of it is still warranted even though more thorough trials are required. A typical dose of the tincture (which is the most effective form in trials, at least compared to encapsulated extracts) is 1–2 mL t.i.d. [21]

Má huáng tāng is a traditional Chinese formula first recorded in the *Shāng Hán Lùn (Treatise on Cold Damage Diseases)* written by Zhāng Zhòng-Jǐng in 220 CE. In Japanese, it's called maō-tō, and in English, ephedra decoction. It has been approved for use in treating influenza in the present era and has been used for this purpose previously. In an open trial, 28 adult Japanese patients diagnosed with influenza were randomized to receive 2.5 g of ephedra decoction as a granulation (essentially a dried, granulated form of the decoction) orally, 75 mg of oseltamivir b.i.d. orally, or 20 mg of zanamivir b.i.d. by inhalation. The ephedra decoction group's median fever duration was substantially lower than that of the oseltamivir group and was also lower than that of the zanamivir group. Regarding the period of viral

persistence within nasal secretions, the median duration of overall symptoms, or the serum cytokine profiles, there was no variation between the groups. There were no side effects, with the exception of one patient getting ephedra decoction and another receiving oseltamivir, both of whom showed slightly elevated serum transaminases. Similar trials including 150 Japanese children with influenza investigated the effects of ephedra decoction in combination with oseltamivir, zanamivir, oseltamivir, and zanamivir alone. In patients with influenza A, the mean duration of fever was considerably lower in the zanamivir and ephedra decoction + oseltamivir groups than in the oseltamivir group; there was no difference in individuals with influenza B. These investigations show that ephedra decoction is as safe and effective as medications that block neuramidase, even if double-blind trials are necessary to validate this. However, the exact mechanisms of action of ephedra decoction remain unknown.

Three plants are added to the combination in the antiwei, an unidentified ephedra decoction version. In a three-day double-blind experiment, 480 Chinese adults with influenza (n = 125) or influenza-like disease (n = 355) were randomized to receive either a placebo or antiwei granulation (6 g b.i.d.) at the same dose. The antiwei group experienced a significant reduction in the duration and severity of confirmed influenza and influenza-like illness as compared to the placebo group. The groups experienced similar negative effects, which were minor.

The Case for Echinacea

A notable illustration of how badly conducted research trials can make a herb that is clinically very beneficial appear useless is *Echinacea angustifolia* (narrow-leaved purple coneflower). This herb was and is greatly lauded in traditional herbalism for VRI. 437 young adult American volunteers with small antibody titers to rhinovirus type 39 were randomly assigned to one of seven groups in a well-known clinical research. After taking their initial therapy for seven days—one of three echinacea extracts in three groups or four separate placebo groups—all individuals were exposed to the rhinovirus. After that, every group that had been taking echinacea switched to a placebo, and three of the groups that had been taking a placebo changed to one of the three preparations of *E. angustifolia*

(so one group, the seventh group, took placebo the entire time). No significant difference was identified among any group in the prevalence of infection, symptom severity, or virus titers at any time in the trial.

A supercritical carbon dioxide extract, a 60% ethanol tincture, or a 20% ethanol tincture were the three extracts that were utilized. Just the 60% extract matches anything that was specifically recognized to be effective before the study, while the first and last extracts are not based on conventional usage. A more significant issue pertained to the dosage: each extract was administered at a rate of just 1.5 mL (or 300 mg of *E. angustifolia* root) t.i.d. This is not nearly as frequently as necessary, and it is at least one-third the effective amount (usually a full 5 mL or 1 tsp of *E. angustifolia* tincture is given at a time) during an acute cold, a typical dose is at least six times per day. The preventative therapy period was just too little to be practical. Since *E. angustifolia* was not administered consistently to any group, it was impossible to determine an efficient dosage schedule through ongoing treatments. The most that can be inferred from all of this is that very low and infrequent dosages of *E. angustifolia* (sometimes in extracts with a historical foundation for usage) are ineffective; this could have been determined without the need for an expensive, large-scale clinical investigation. This study is frequently used to support the idea that *E. angustifolia* is ineffective, but at the very least, it should be used to support the case for higher, more regular doses.

Evidence from earlier clinical trials suggests that the dose employed in this trial was insufficient. A 500 mg capsule of *E. angustifolia*, together with 250 mg of *E. purpurea* and 250 mg of *E. pallida*, was given six times a day to 148 American college students as part of a 2002 double-blind trial. The results showed that the capsule was no more beneficial than a placebo. It is utterly puzzling that even less material was used by the researchers in the 2005 trial. It should come as no surprise that the majority of experiments support the idea that modest, infrequent doses of the herb do not aid in accelerating recovery from VRIs, as the majority of other trials have employed *E. purpurea*, an inferior species, for this purpose. Gargling with echinacea products is also highly significant because of its topical numbing action, which is quite beneficial in relieving pharyngeal pain.

It has been demonstrated that some echinacea species regulate inflammation in cells infected with respiratory viruses such as rhinovirus and influenza. This effect may assist prevent cytokine storms as well as elucidate lessening of symptoms.

Formulating for Acute VRI

Developing a customized regimen is the true skill in treating patients with acute VRIs. A proposed base formula, this needs to be modified to meet each patient's unique needs. Add the *Sambucus* spp. fruit if they are determined to have influenza or if the illness is highly likely. If their oral temperature is higher than 103°F, add febrifuge herbs like the bark and/or leaves of *Salix* spp. (willow) or *Betula* spp. (birch) or, in the worst situation, boiled root of *Aconitum* spp. (aconite). In the event that the patient has extremely severe myalgia, these herbs or other analgesics are also recommended. They should take the diaphoretic tea as prescribed in addition to adding *Zingiber officinale* (ginger) rhizome or another heating herb if they do not have a fever. To allow the echinacea, which should make up 30% of the mixture, to have its numbing effect, the formula should be gargled if the patient has a sore throat. In case the flavor of the mixture is too strong, *Nepeta cataria* (catnip) glycerite, at a ratio of 40%, can be used in place of heal-all, with desert parsley being restricted to 10%. A mucolytic herb, such as the flower buds of *Grindelia* spp. (gumweed), the leaves of *Eriodictyon* spp. (yerba santa), or the resin of *Populus* spp. (poplar), should be administered if the patient has a bothersome wet cough. If the patient has a persistent dry cough, an antitussive such as the bark of *Prunus virginiana* (wild cherry) or *Tussilago farfara* (coltsfoot) should be administered in addition to a mucolytic herb.

Take 1 tsp three times a day for three days, or every two to four awake hours after that. If fever is more than 101°F, add any of the diaphoretic herbs to hot tea.

Preventing VRI

Herbs also have substantial ability to help reduce VRI in the first place. Here are several botanical extracts that have been demonstrated in clinical trials to have this effect.

The immunomodulating plants *Panax ginseng* (Asian red ginseng) and *P. quinquefolius* (American ginseng) have both been investigated quite extensively for their potential to prevent VRI. At the onset of the influenza season, 100 adults from Korea were randomly assigned to either a red ginseng extract or a placebo in a double-blind trial. The standardized Asian red ginseng extract contained 7 mg/g of the combined ginsenosides Rg1 and Rb1. It was administered at a dose of 1 g t.i.d.

When comparing the Asian red ginseng group to the placebo group, the incidence of VRI was much lower (reduced by around 45%). In individuals who acquired VRI, there were no appreciable differences in the severity or length of illness across the groups. In this study, Asian red ginseng was just as safe as a placebo. In a double-blind trial, 227 adult Italian recipients of influenza vaccination were given an alternate extract of Asian ginseng at a dose of 100 mg daily, and after four weeks of supplementation, the extract was compared to a placebo. The incidence of overall VRI was considerably lower in the vaccine + ginseng group than in the vaccine + placebo group after an extra eight weeks of treatment. Asian ginseng intake resulted in considerably greater influenza antibody titers and natural killer cell activity as compared to placebo. There were very few, moderate side effects.

An American ginseng extract standardized to include 80% polysaccharides and 10% protein from roots of the plant was tested in multiple double-blind clinical trials. During the start of the influenza season, 279 Canadian adults were randomly assigned to receive either 400 mg of American ginseng extract or a placebo for a period of four months. Compared to the placebo group, a considerably less number of volunteers in the American ginseng group experienced more than one VRI and a significantly smaller number experienced no VRI at all. In comparison to the placebo group, the American ginseng group experienced much less severe and prolonged VRI symptoms.

Using the same American ginseng extract at a dose of 200 mg b.i.d., 198 older American individuals in assisted-living and nursing homes were compared to a placebo for a period of 12 weeks. When compared to the placebo group, the American ginseng group had a significant decrease in laboratory-confirmed instances of influenza and RSV infection, although there were no differences in side effects. A study of forty-three senior

American individuals living in the community who received the influenza vaccination verified the use of the same American ginseng extract at the same dose in a very similar trial design. In this trial, there was a very substantial difference between the American ginseng group and the placebo group in terms of the incidence and duration of VRI. Asian and American ginseng appears to be very promising in lowering the incidence of VRI throughout the winter, based on all of this research.

The use of American ginseng to treat acute VRI has not received much research. In a randomized experiment, 46 Canadian children with acute VRI, ages 3 to 12, were given a liquid standardized extract of American ginseng or a placebo. The dosage was weight-based and complex: on days 1, 2, and 3 of their VRI, one group received 26 mg/kg, another group received 17 mg/kg, and a third group received a placebo. A second group received half of this dose. Three pieces of each dose were given throughout the day. Not only were there no differences in the length or intensity of VRI symptoms across any of the groups, but there was also no variation in side effects. This is significant because, according to Chinese medical philosophy, it is possible that an adaptogenic or qi-tonifying herb, like American ginseng, will exacerbate VRI by "tonifying the pathogen." In actual use, this effect was not observed. It does, however, also imply that other herbs, as previously said, are preferable for this purpose and that American ginseng is not likely to be very helpful in treating VRI.

According to epidemiologic data, children in Japan who consume more Camellia sinensis, or green tea, have decreased incidence of influenza. A big epidemiological study in Japan found that any level of green tea consumption is connected with a substantial reduction in the risk of influenza-related death in women, but not in males.

In an open-label experiment involving 757 Japanese youths, gargling green tea three times a day did not prove to be any more helpful than water for avoiding influenza. A green tea extract containing 378 mg of catechins and 210 mg of theanine per day significantly outperformed a placebo in a double-blind trial including 197 Japanese individuals who cared for the elderly in medical institutions in terms of lowering the incidence of VRI. Laboratory-confirmed influenza rates appeared to be similar in all groups,

suggesting that the main effect of the green tea product was prevention of other viral illnesses. A second green tea extract comprising epigallocatechin gallate and theanine was tested against a placebo (one capsule taken once a day, milligram dose unknown) in a separate double-blind trial with 108 adult Americans. The trial lasted three months. When compared to a placebo, the green tea extract dramatically reduced the overall incidence, severity, and duration of VRI. The green tea extract dramatically raised levels of γδ T cells, which are thought to be essential for warding off influenza, as compared to a placebo. The course of treatment was extremely safe.

Over the course of 12 weeks, during the height of the cold and flu season, 146 adult British subjects were randomized to receive a garlic supplement or a placebo in a double-blind trial. The garlic product was used once day and included 180 mg of a powder that included allicin. With around one-third as many colds in the garlic group as in the placebo group, self-reported VRIs were considerably less common in the garlic group. When comparing the garlic group to the placebo group, there was a substantial decrease in both the severity and duration of VRI symptoms. Although there hasn't been any other research on the use of garlic to prevent VRI, it seems like a relatively simple solution considering its safety and possible effectiveness.

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CHAPTER 4

HERBAL TREATMENTS FOR CNS DISEASES BY VIRUS AND ITS HERBAL CURE

DR. SUKIRTI UPADHYAY

About 0.5–2% of all live births have congenital cytomegalovirus (CMV) infections, which are the most prevalent congenital infections worldwide and can result in either early or late severe neurological and neurosensorial impairment. To enhance the neurodevelopmental and auditory outcomes of symptomatic newborns, ganciclovir (GCV) and its oral pro-drug, valganciclovir (val-GCV), are increasingly being administered, even though no medication has been approved for the therapy of congenital CMV infection. Although they have only been used in a small number of instances, foscarnet and cidofovir are additional potentially effective treatments for congenital CMV illness. To find evidence-based or scientific publications assessing the pharmacokinetics, effectiveness, and side effects of GCV/val-GCV and the other two antiviral medications, a literature search was conducted. [1]

The herbal solution to these diseases is still pending.

Meningitis and its Herbal Cure

Meningitis is a condition characterized by swelling of the membranes surrounding the brain and spinal cord. Usually, a bacterial or viral infection of the fluid around the brain and spinal cord causes the swelling. Meningitis can also be caused by wounds, cancer, some drugs, and other infections.

Researchers assessed the impact of co-therapy with Yin-Chen Extract and albendazole on eosinophilic meningitis produced by Angiostrongylus

cantonensis in BALB/c mice. Worm recovery, the fourth ventricle's histological score, tissue-type and urokinase-type plasminogen activators, matrix metalloproteinase-9, total protein in the cerebrospinal fluid, leukocyte counts, and proinflammatory cytokines are assay indications for the treatment impact. Consequently, co-therapy with albendazole and Yin-Chen-Extract considerably reduced ($P < 0.05$) these parameters. While Yin-Chen-Extract might have pharmacologic properties that help suppress parasite-induced inflammation, many of these potential advantages need to be verified by science before being used. According to this study, albendazole and Yin-Chen-Extract work well together. [3]

Nipah and its herbal cure

The Nipah virus, a paramyxovirus that mostly affects Pteropus bats in the wild, was initially identified in 1998 during a widespread case of severe encephalitis in Malaysia among individuals who came into contact with infected pigs. It seems that the virus infected one or more pigs from bats, and it then effectively transmitted from pig to pig and ultimately from pigs to humans. Since 2001, outbreaks of the Nipah virus have been identified in Bangladesh almost annually and sporadically in neighboring India. Over 70% of people infected have died during outbreaks in Bangladesh and India, which are marked by recurrent person-to-person transmission. Nipah has a very high mutation rate due to its RNA virus nature. If a human-adapted strain were to contaminate communities in South Asia, the virus would spread swiftly due to high population density and global connectivity. The Nipah virus has several traits that make it more likely to spread over the world and cause a pandemic. Besides, they are already vulnerable. Research on the genetic and molecular underpinnings of henipavirus respiratory transmission, improved surveillance for human infections, support from affluent countries to decrease the hazard of infectious agent transmission between people in low-income healthcare settings, and vaccination thoughtfulness in communities continuously at threat of exposure to infectious agents.[4]

Infections with the Nipah virus (NiV) are extremely contagious and can result in severe febrile encephalitis. High fatality rates from an outbreak of NiV infection have been documented in Bangladesh, East Timor, Malaysia,

Papua New Guinea, Vietnam, Cambodia, Indonesia, Madagascar, Philippines, Thailand, and India, among other Southeast Asian nations. NiV was designated as an emerging priority disease by the World Health Organization (WHO) due to the increased potential of an epidemic breakout. Unfortunately, there are no FDA-approved medications or effective treatments available to treat this infection. Glycoprotein, one of the nine proteins of NiV that are known to exist, is crucial for the virus's initial entrance and attachment to host cell receptors. In this case, 79,892 chemical entities from three antiviral databases have been computationally tested against NiV glycoprotein (NiV-G). In particular, several steps have been taken in the process of initially identifying possible NiV-G inhibitors, including multi-step molecular docking, extensive molecular binding interactions investigation, binding free energy estimation, in silico pharmacokinetics, synthetic accessibility, and toxicity profile evaluations. Furthermore, to comprehend the dynamic characteristics of the NiV-G protein coupled to the five inhibitors (G1–G5) that have been proposed, their behavior in contacts, and any conformational changes in the NiV-G protein during simulations, molecular dynamics (MD) simulation has been carried out. Additionally, from all MD simulation trajectories, binding free energies (ΔG) based on the Poisson-Boltzmann Surface Area (MM-PBSA) have been calculated to comprehend the energy contribution of each suggested molecule in preserving and stabilizing the complex binding interactions with NiV-G. The proposed compounds exhibited a considerable affinity towards the NiV-G protein, as evidenced by their high negative ΔG values, which ranged from −166.246 to −226.652 kJ/mol. [5]

The phytoconstituents quercetin (73%), baccatin III (71%), psoralen (67%), embelin (65%), menisdaurin (64%) and azadirachtin (62%), lupeol (52%), rutin (47%), β-sitosterol (43%) and hesperidin (41%) are reported to be useful for treatment.

Despite having strong anti-HBV efficacies, interferons (like IFN-α) have negative side effects, and nucleoside analogs (like lamivudine) cause drug resistance to develop. In contrast, a variety of plant-based or natural products have demonstrated comparable or even greater efficacy. Therefore, novel antiviral approaches need to concentrate on both synthetic and maybe natural substances. By integrating in vitro cell culture and silico molecular

docking techniques, we have evaluated the unique anti-HBV activity and defined the inhibitory mechanism of numerous plant-derived pure compounds of distinct classes in this study. Out of the twelve non-cytotoxic chemicals tested (ranging from 2.5 to 50 μg/ml), ten (10 μg/ml) were shown to maximally reduce HBsAg production during the day. Comparing quercetin (73%), baccatin III (71%), psoralen (67%), embelin (65%), menisdaurin (64%) and azadirachtin (62%), which showed significant suppression of HBeAg production, to luteol (52%), rutin (47%), β-sitosterol (43%) and hesperidin (41%), the last four showed only modest efficacies against HBV replication. The highly effective compounds enhanced further assessment of quercetin's anti-HBV characteristics. Lamivudine's docking revealed a robust interaction with the simulated HBV Pol active site. Similarly, every docked antiviral drug and HBV Pol generated extremely stable complexes (ΔG =−6.1 to −9.3 kcal/mol). When considered collectively, the findings point to the tested natural chemicals' potential as novel viral Pol/RT inhibitors with anti-HBV properties. [6]

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CHAPTER 5

HERBAL TREATMENTS FOR VIRAL DISEASES CAUSING FEVER

DR. SUKIRTI UPADHYAY

A virus is the source of the severe and frequently fatal disease Ebola. Fever, vomiting, diarrhea, blood, and frequently even death are among the symptoms. Both humans and other primates (chimpanzees, gorillas, and monkeys) can contract Ebola.

The ongoing Ebola pandemic outbreaks in Africa have caused panic attacks all across the world. In locations where the virus has spread, the mortality rate among Ebola-infected individuals is substantial (30–70%). Despite these atrocities, there were few medicinal drugs or choices available to help combat this lethal viral disease. Therefore, it is necessary to bring back into the global market several patented agents, biotherapies, or prophylactic/therapeutic vaccinations. These include patents on small molecular compounds, short DNA/RNA sequences or oligomers, chemical links with biomolecules, herbal medicine, and so forth. Furthermore, research is being done on these therapy approaches' potential mechanisms of action. This review outlines the various characteristics of Ebola infections, including their genesis, pathologic progression, genetic alterations, therapeutic context, and economic considerations, to support Ebola biomedical research. [1]

There isn't an approved antiviral medication on the market right now to treat or prevent Ebola virus (EBOV) infection. In order to search for anti-EBOV-GP agent(s), we described an EBOV-glycoprotein (GP) pseudotyped HIV-1-based vector system in several cell cultures, including human macrophages

and umbilical vein endothelial cells (HUVECs). The following plants have been proven to be useful in therapy:

a) ***Prunella vulgaris***

Using this approach, we were able to show that an aqueous extract (CHPV) from the Chinese herb Prunella vulgaris exhibited a strong inhibitory effect against the infection of multiple cell lines, including HUVEC and macrophage, by the EBOV-GP pseudotyped virus (EBOV-GP-V). Furthermore, our findings showed that CHPV could prevent infection of VeroE6 cells with the eGFP-expressing Zaire ebolavirus (eGFP-ZEBOV). It was shown that CHPV's anti-EBOV activity was dose-dependent. At a concentration of 12.5 μg/ml, the CHPV displayed a greater than 80% suppression of eGFP-EBOV and EBOV-GP-V infections. According to our research, CHPV inhibited EBOV-GP-Vs by directly attaching to them and preventing early viral activities. It's interesting to note that our findings demonstrate that CHPV can boost the monoclonal antibody MAb 2G4's anti-EBOV activity against EBOV-GP. In summary, this research indicates that CHPV exhibits anti-EBOV properties and could be utilized as an innovative antiviral strategy to combat EBOV infection.[2]

b) ***Rhodiola rosea***

Due to the high fatality rates of Ebola virus infections and the lack of an FDA-approved vaccine or medication for prevention and treatment, the recent West African Ebola virus pandemic of 2014–2016 highlights the need for the development of innovative anti-Ebola medicines. A vast reservoir of bioactive compounds is found in traditional Chinese medicines (TCMs), and numerous TCMs have been demonstrated to have antiviral properties. A high throughput experiment was used to assess 373 extracts from 128 TCMs to look for agents that prevent the entry of Ebola virus cells. *Rhodiola rosea* extract showed strong and specific suppression of the Marburg and Ebola viruses' ability to enter cells. Additionally, *Rhodiola rosea*-derived commercial products were assessed utilizing the pseudotyped Ebola virus entry assay Furthermore, the pseudotyped Ebola virus entry assay was used to assess twenty commercial compounds extracted from *Rhodiola rosea*. The results indicated that two structurally related

compounds, gallic acid and ellagic acid, are the most effective. Using an infectious Ebola virus, the extract's and the two pure chemicals' activities were verified. The results of the time-of-addition assays indicate that the *Rhodiola rosea* extract and the active ingredients function early in the infection cycle, after the first cell attachment but before the fusion of the viral and cell membranes. Based on our research, *Rhodiola rosea* may be developed as a novel anti-Ebola medication due to its strong anti-filovirus capabilities. [3]

Dengue and its herbal cure

A virus that is carried by mosquitoes and spreads quickly, dengue is extremely dangerous for people's health. When there are no effective medications or vaccinations, further resources should be looked into. A growing body of research indicates that plants provide an abundant source for the development of safe antiviral drugs for human use. Because plants are rich repositories of chemically varied chemicals, the process of discovering new drugs based on plants is intricate and time-consuming. Numerous in silico techniques can simplify and reduce the cost of this operation. Therefore, in order to screen possible candidates against dengue, we used molecular docking, pharmacophore mapping, molecular dynamics (MD) simulations, and ADME (absorption, distribution, metabolism, excretion) prediction. In particular, the potentially active compounds from a ligand library were prioritized using a combination of molecular docking and pharmacophore mapping. 3D-QSAR pharmacophore modeling was used to predict the biological activities of ligands derived from plants. Using molecular docking, interactions between the following proteins were examined: envelope G protein, NS2B/NS3 protease, NS5 methyltransferase, NS1, NS5 polymerase, and active plant-based ligands (pIC50 > 5.1). The optimal docked complexes, namely NS1–mulberroside A, NS5 methyltransferase–punigluconin, NS5 methyltransferase–chebulic acid, NS2B–NS3 protease–curcumin, and envelope G protein–mulberroside C, were further studied using MD simulations to evaluate fluctuations and conformational changes during protein-ligand interaction. Studies on ADME were conducted to evaluate its drug-like qualities. Altogether, these in silico findings assisted in identifying putative plant-based hits against

several dengue viral receptors, which can then be confirmed through bioactivity-based experiments.[4]

Dengue is a virus that is spread by arthropods. The anti-malarial drug chloroquine, anti-inflammatory drugs like prednisolone and lovastatin, iminosugar, celgosivir60, anti-parasitic drug ivermectin, nucleoside analog, balapiravir, and others have all been tested against dengue during the last ten to twelve years; however, none of them have been developed as a potential drug candidate against DENV. When the small molecule/drug candidates did not show the desired results in clinical trials, researchers looked to natural materials called phytochemicals to develop dengue-fighting medicinal agents. To date, over 70 medicinal herbs have been found to exhibit anti-DENV properties when their extracts and purified compounds are used. The worldwide occurrence of dengue fever (DF) has made it a global health concern because of its high fatality and morbidity rates, particularly in tropical and subtropical areas. *Aedes aegypti* and *Aedes albopictus* mosquito are carriers of the Dengue virus. Regretfully, there is now no licensed vaccine or effective anti-dengue medication to treat viral infections. Scholars have focused on therapeutic plants to find natural chemicals with anti-dengue properties. Consequently, we are concentrating on therapeutic plant extracts since they might be safer, more potent, and less hazardous than manufactured medications. The active ingredients of 35 medicinal plants having anti-dengue properties, together with a brief description of each plant, are listed in the current review paper. The results of this investigation will be useful in proving that natural products could be a good source of novel anti-dengue chemicals.

Globally, there is worry about dengue fever (DF). Single-stranded positive-sense RNA virus Dengue virus (DENV) belongs to the genus Flavivirus and family Flaviviridae. It is spread via the bite of female Aedes aegypti and Aedes albopictus mosquitoes carrying the infection. The DENV genome is about 11 kilobases long. Worldwide reports of DENV have identified four distinct serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. Recently, the DENV-5 serotype has also been identified. [4] One open reading frame in the DENV genome encodes seven distinct nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) as well as three structural components (the capsid, premembrane, and glycoprotein envelope. Studies

have shown that infections with DENV-1 and DENV-3 are more dangerous than those with DENV-2 and DENV-4, Dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) are three different types of DENV illness. Five percent of the individuals had severe DHF and DSS, while the remaining ninety-five percent of cases had normal DF. DF begins when it's rainy and wet outside. The water accumulates in coolers, ponds, playgrounds, and open spaces to give a suitable situation for A. aegypti mosquito reproduction. Because of its intense muscular aches and bodily agony, DF is sometimes referred to as "break-bone" fever. Another major issue is dengue, which is an antibody-dependent enhancement (ADE). When a person contracts one serotype of dengue, it can have a devastating impact on subsequent infections with heterologous strains of the virus and potentially result in DHF/DSS. Due to its ADE, there aren't any licensed vaccines that are currently effective against DENV. According to data from the World Health Organization (WHO), there are over 100 million cases of DF and 500,000 cases of DHF worldwide. Approximately 18,000 deaths are also documented annually. Dietary fiber and naturally occurring bioactive substances provide health advantages and illness prevention. Papaya by-products make up 20–25% of the fruit's weight, and they're a good source of fiber, minerals, and phenolic compounds with a variety of pharmacological uses. The present study's findings demonstrated the antioxidant, flavonoid, and phenolic properties of papaya peel powder and paste. When compared to control chapathis, the antioxidant activity rose as the concentration of the processed papaya peel increased. PSP and PPP had IC50 values of 0.11 and 0.18 mg/ml, respectively. With IC50 values of 0.60, 0.37, and 0.35 mg/ml for the control chapathi, PSC, and PPC, respectively, it was evident that heat treatment had little effect on papaya peel.

Artemisinin

Investigating the antiviral activity of artemisinin against flaviviruses has been conducted using as an *in vitro* model bovine epithelial cells from embryonic trachea (EBTr) contaminated with the cytopathic strain Oregon C24V of bovine viral diarrhea virus (BVDV), a member of the Flaviviridae family. Artemisinin is a safe medication derived from *Artemisia annua* and commonly used to treat malaria. The degree of protection towards the

cytopathic effect of BVDV on host cells and the decrease in BVDV-RNA release into the culture medium were used to measure the antiviral activity. Before being incubated with virus-free conditions for 72 hours, EBTr cells were exposed to BVDV for 48 hours in order to cause an intermediate cytopathic impact in the untreated cells. Up to 100 μM of ribavirin and artemisinin did not cause any toxicity in the host cells; however, IFN-α caused a little amount of toxicity at doses greater than 10 U/mL and up to 100 U/mL. BVDV-induced cell death was significantly decreased when IFN-α, ribavirin, and artemisinin were administered to infected cells. These medications worked in concert to produce an additional protective effect. These medications significantly reduced the amount of BVDV virions that infected EBTr cells produced or released, and when combinations of these medications were tested, there was a further benefit. These findings point to the potential benefit of using artemisinin in conjunction with the available pharmaceutical treatments.[5]

Rosmarinic acid (RA)

Dietary fiber and naturally occurring bioactive substances provide health advantages and illness prevention. Papaya by-products make up 20–25% of the fruit's weight, and they're a good source of fiber, minerals, and phenolic compounds with a variety of pharmacological uses. The present study's findings demonstrated the antioxidant, flavonoid, and phenolic properties of papaya peel powder and paste. When compared to control chapathis, the antioxidant activity rose as the concentration of the processed papaya peel increased. PSP and PPP had IC50 values of 0.11 and 0.18 mg/ml, respectively. With IC50 values of 0.60, 0.37, and 0.35 mg/ml for the control chapathi, PSC, and PPC, respectively, it was evident that heat treatment had little effect on papaya peel.[6]

Probiotic bacteria for viral infections

Probiotic bacteria have been demonstrated in numerous intervention trials to be effective against HIV- and rotavirus-induced diarrhea. Despite this, probiotic bacteria's antiviral properties have not yet been thoroughly investigated. Probiotics and other lactic bacteria, together with their metabolic products, were administered in several experimental designs to

non-tumorigenic porcine intestinal epithelial cells (IPEC-J2) and alveolar macrophages (3D4/2). The study employed the vesicular stomatitis virus (VSV) as a model virus. Viral inhibition and cell survival were assessed using an antiviral test, and immunofluorescence was used to corroborate the results. Viral infectivity was lowered by up to 60% when probiotic bacteria were pre-incubated with cell monolayers. By directly attaching VSV to their surface, all of the bacteria were able to inhibit VSV binding to the cell monolayers. Other lactic bacteria and probiotics inhibited viral Hindering the adsorption and cell internalisation of the VSV due to the straight trapping of the virus by the bacteria, "cross-talk" with the cells in confirming the antiviral protection and creation of metabolites with a direct antiviral effect.[7]

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CHAPTER 6

HERBAL TREATMENTS FOR LIVER DISEASES CAUSED BY VIRUS

DR. SUKIRTI UPADHYAY

In a study, the kinetics of WHV infection in woodchucks in the liver and the five major lymphoid organs (lymph nodes, spleen, thymus, bone marrow, and peripheral blood lymphocytes). Groups of woodchucks that had been experimentally infected with a standardized WHV inoculum were sacrificed at different times during the 65-week virus's acute phase, which lasted until either the development of chronic infections or the eventual hepatocellular carcinoma or until the period of serologic recovery. WHV infection impacted not only the liver but all major lymphoid system components during the course of the infection. A complicated set of kinetic patterns for the development of WHV DNA in the liver and different lymphoid tissues were observed during the viral infection. In order of organ discovery, the liver, spleen, lymph nodes, peripheral blood lymphocytes, and thymus came next. There were several differences in the cellular WHV DNA patterns of acute WHV infection patients and those who recovered serologically. Based on findings collected for this study, the host lymphoid system is important for the natural history of hepadnavirus infections from the very beginning of virus entrance.[1]

Hepatitis is a dangerous disease that is common all over the world and often sparks epidemics. This zoonotic disease results in lethargy, anorexia, jaundice, and finally death. Although vaccines against hepatitis A and B have been developed, it is challenging to develop immunizations against other prevalent hepatitis strains that are equally harmful and spread around the world. Because natural products originating from live organisms and

found freely in nature contain bioactive chemicals with considerable pharmacological capabilities, they have shown efficacy against different kinds of hepatitis. These are natural goods that are easy to use or eat and don't do too much harm to the body. Our main topic of discussion is the opportunistic pathogen known as the hepatitis E virus (HEV), which can cause severe jaundice. People who have compromised immune systems, including youngsters, the elderly, organ transplant recipients, and pregnant women, are the main targets of this virus. It is more prevalent in underdeveloped countries with poor hygiene conditions. A patient who has HEV infection is more susceptible to contracting other viruses and HIV. In this review, we discussed the natural protein lactoferrin, which is derived from milk colostrum, and certain extracts of medicinal herbs that have been demonstrated to be effective in treating various forms of hepatitis. significant advancements in pharmaceutical science, contemporary pharmaceutical discoveries and modern medicine are based on these kinds of natural therapies.[2]

It has been demonstrated that the following plants work well in therapy:

Phyllanthus Family

It has been suggested that herbs in the Phyllanthus family contain antiviral qualities. Therefore, the effects of three different Phyllanthus extracts on the serologic state of 123 patients with chronic hepatitis B. Eleven patients were administered an extract of *Phyllanthus amarus* (L) by S.P. Thyagarajan of Madras, India. 42 patients received an extract of *Phyllanthus urinaria* (L) from Henan Province, China, while 35 patients received *Phyllanthus niruri* (L) from the same province. Thirty-five patients in the control group did not get herbal therapy. Patients receiving *Phyllanthus urinaria* (L) were more likely to lose detectable hepatitis B e-antigen from their serum and to seroconvert hepatitis B than patients getting either of the other two preparations. Compared to patients receiving either of the other two preparations, those receiving *Phyllanthus urinaria* (L) had a higher chance of both losing detectable hepatitis B antigen from their serum and seroconverting hepatitis B e-antibody status from negative to positive. Regarding the hepatitis B s-antigen, no patient's status changed.[3]

Radix flavescentis Sophorae

A species of plant in the Fabaceae family's genus Sophora is the shrubby sophora, also known as *Sophora flavescens*. This genus, which is widely dispersed throughout Asia, Oceania, and the Pacific islands, is made up of about 52 species, 19 variations, and 7 forms.

10 randomized clinical trials with a total of 898 individuals were included. We were highly biased while evaluating each trial. During a follow-up period of one to twelve months, Radix *Sophorae flavescentis* was examined in oral capsules, intramuscular injection, intravenous infusion, and acupoint (a specific acupuncture location) injection. Adefovir, lamivudine, interferon, tiopronin, thymosin, and other Chinese herbs were among the drugs that were being compared. Trials involved children as young as 14 years old.

People with chronic hepatitis B had cirrhosis in one study. Trials on morbidity, mortality from all causes, quality of life-related to health, major adverse events, and mortality associated with hepatitis B were not available. There is insufficient evidence to determine whether Radix *Sophia eflavescentis* has a significant effect on the proportion of participants with detectable HBV-DNA (RR 1.14, 95% CI 0.81 to 1.63; I2 = 92%; 8 trials, 719 participants; very low-certainty evidence) or adverse events deemed "not to be serious" (RR 0.86, 95% CI 0.42 to 1.75; I2 = 0%; 2 trials, 163 participants; very low-certainty evidence). The percentage of individuals in Radix Sophorae flavescentis (7 trials, 588 participants; extremely low-certainty evidence; RR 0.86, 95% CI 0.75) who had detectable hepatitis B virus e-antigen (HBeAg) dropped. = 43%).[4]

In order to uncover efficient anti-HCV drugs, 20 Chinese herbs that are commonly used for dispersing toxins and clearing heat were screened using a model of hepatitis C virus (HCV) infection in nude mice. A transmission electron microscope was used to look for the presence of HCV-like particles in human fetal hepatocytes transplanted into mice's spleens after the model mice were treated with a particular medication for three months. The quantitative RT-PRC method was also used to measure the amount of HCV-RNA in the serum both before and after therapy. Following therapy, all of

the model mice had HCV-like particles. The serum level of HCV-RNA dropped following treatment with Radix Gentianae, Radix Scutellariae, Radix Sophoraetonkinensis, Fructus Gardeniae, and Fructus Sophoraeflavoscentis.

However, after receiving other medications, it remained unchanged. While none of the 20 herbs that were screened were effective in eliminating HCV, *Radix Gentianae, Radix Scutellariae, Radix Sophoraetonkinensis, Fructus Gardeniae, and Fructus Sophoraeflavoscentis* were found to be highly effective in inhibiting HCV-RNA replication. [5]

Hepatitis B

The small DNA virus known as hepatitis B virus (HBV) primarily damages the liver. Prolonged HBV infection can lead to such liver disorders as cirrhosis, hepatocellular carcinoma, and chronic hepatitis. The HBV enhancer composition appears to have adopted a regulatory mechanism particular to the primary hepatic metabolic genes since it links dietary cues that regulate hepatic glucose and fat metabolism in the liver to HBV gene expression and replication. We call this unique virus-host interaction the "metabolovirus model" because it is mediated by hepatic metabolic processes. Our view is that HBV cleverly leverages the host's resources to ensure its survival by imitating the appearance of key genes involved in glucose homeostasis. More specifically, the virus prevents potential host resistance by enlisting transcription factors and coactivators shared by essential hepatic metabolic genes.

This also guarantees the virus's prompt and appropriate response to changes in its metabolic milieu. Moreover, we forecast a variable nature of HBV gene expression by combining its gene expression with the representation of hepatic metabolic genes that change throughout the day. In addition to other immune-evading tactics the virus has used, like the secretion of the e antigen, this can help it in its attempts to evade the host immune system. We propose new mechanisms to explain clinical phenomena that were previously unexplained, such as the observed variation in disease rigorousness between different geographical areas with different nutritional habits, based on our "metabolovirus model." Furthermore, we propose that HBV-positive individuals should strictly refrain from short-term starvation

and follow dietary guidelines like consuming complex carbohydrates before bedtime due to the up-regulating effect of food deficiency on HBV gene expression and replication. Thus, by regulating food intake, our theory paves the way for viral manipulation and creates new opportunities for the use of nutritional or food therapy as an efficient anti-HBV tool.[6]A herbal remedy for these illnesses is still pending.

Both technical and practical challenges have made it more difficult to identify and develop novel antiviral agents that can be used to treat hepatitis C virus (HCV) infection. It is difficult, if not impossible, to grow HCV virions in vitro using any reliable techniques. A major advancement that has made it possible to conduct extensive screening to find HCV intracellular replication inhibitors is the development of HCV RNA replicons. However, drug screening programs and mechanism of action studies based solely on these assays will not identify compounds targeting either early (virion attachment, entry, uncoating) or late (virion assembly, egress) stages of the viral replication cycle, since replicons do not go through a complete replication cycle. HCV RNA replicons will also not be used to identify medications that adversely impact the infectivity of new virions. Similar in structure to HCV, the bovine viral diarrhea virus (BVDV) also typically causes chronic, long-term infections in the hosts that it infects. Because the BVDV surrogate model is based on a virus, it is appealing. The virus replicates itself once, is simple to culture in vitro, and can be studied genetically using molecular clones. Similar to HCV, BVDV enters cells through the LDL receptor, uses the internal ribosome entry site (IRES) for translation, has a similar NS3 helicase/NTPase, a mechanistically similar NS5B RNA-dependent RNA polymerase, and appears to have an equivalent mechanism for virion maturation, assembly, and egress. It also uses an NS4A cofactor with its homologous NS3 protease. Even though the concordance between medications active in HCV and BVDV is currently mostly unknown, BVDV is still a widely used model system for assessing medication efficacy against HCV as well as for investigating drug mechanisms of action.[7]

Long-standing obstacles to the analysis of the hepatitis B and hepatitis C viruses include the absence of an appropriate small animal model. The two viruses could only be investigated in chimpanzees or humans. A novel

chimeric mouse model that was permissive to HBV and HCV infection was recently created. In this prototype, primary human hepatocytes are transplanted early after birth into uPA+/+-SCID mice that have a transgene-induced liver disease. Without sacrificing their regular metabolic processes, these human hepatocytes gradually regenerate the injured mouse liver by integrating into the parenchyma. After transplantation, mice can contract HBV and HCV infections.

In this review, we go into greater detail about the features of this chimeric mouse model and provide an overview of how it has already aided in the development of novel antiviral drugs for the treatment of viral hepatitis.[8]A herbal remedy for these illnesses is still pending.

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CHAPTER 7

HERBAL TREATMENTS FOR VIRAL DISEASES OF THE SKIN

DR. PRASHANT UPADHYAY

Measles is a serious virus-borne sickness that is extremely contagious, can spread through the air, and can have fatal complications. The measles immunization saved 56 million lives between 2000 and 2021.

Despite the availability of a reliable and reasonably priced vaccination, measles nonetheless claimed the lives of an estimated 128 000 individuals globally in 2021. Most of these deaths involved children under five who had either insufficient or no vaccinations.

By the time they turned one year old in 2021, 81% of children globally had received one dose of the measles vaccine through regular health care, the lowest percentage since 2008.

Overview

Measles is a highly contagious and lethal infection. Before the measles vaccine's development and widespread usage in 1963, severe outbreaks that occurred about every two to three years were thought to cause 2.6 million deaths annually.

Even with a safe and reasonably priced vaccine, measles nonetheless claimed the lives of an estimated 128,000 individuals in 2021, most of them young children.

The paramyxovirus family of viruses responsible for measles usually spreads by airborne and direct contact. The virus infects the body through

the respiratory system and then proceeds to produce severe disease, complications, and fatalities.

A vaccine might make it simple to avoid a deadly viral infection in young children.

When you sneeze or cough, respiratory droplets are released, and it takes 10 to 14 days after exposure for measles symptoms to manifest. These consist of a fever, sore throat, runny nose, irritated eyes, cough, and a red, splotchy rash on the skin.

An established measles infection cannot be cured; however, vitamin A or over-the-counter fever reducers may help with symptoms.

Angiosperm plant for Measles

Twenty-three plant species belonging to 18 Angiosperm families were said to possess curative properties for the cure of measles among the local populace. Amongst the most frequently used plants are *Elytraria marginata* Vahl, *Peperomia pellucida* (L.) Humb., Bonpl. & Kunth, *Vernonia amygdalina* Del., *Momordica charantia* L., *Newbouldia laevis* (P. Beauv.) Seem. ex Bureau, and *Ocimum gratissimum* L.[1]

Shengma-Gegen-Tang

Shengma-Gegen-Tang has been used for many years to treat human peripheral blood mononuclear cells (PBMC) and Vero cells for the measles virus. Compared to Vero cells, the anti-measles activity of 100 μg/ml Shengma-Gegen-Tang in PBMC is much higher. Shengma-Gegen-Tang considerably inhibits the virus's release in PBMC after eight days of infection. Additionally, Shengma-Gegen-Tang preferentially stimulates TNF-α production in PBMC. Time kinetic analysis indicates that secretion was induced rapidly and became apparent within two hours of the PBMC treatment. Reaching its climax took eight to twelve hours. These findings suggest that lymphocytes are necessary for this drug to increase its anti-measles virus action and that TNF-α may play a role in this process. [2]

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CHAPTER 8

MISCELLANEOUS

DR. SUKIRTI UPADHYAY

Some viral infections have multiple symptoms and are not restricted to a particular organ system so they are studied as miscellaneous.

1)The ZIKA Virus and its herbal cure

The Zika virus (ZIKV) is currently emerging as a pandemic. Antiviral therapies are desperately needed, even though the condition is usually asymptomatic. Severe neurologic symptoms following congenital infection in fetuses and infants. The following treatments have some positive effects against ZIKV

Adenosine analog BCX4430

The adenosine analog BCX4430 exhibits strong *in vivo* activity against the Marburg, Ebola, and yellow fever viruses, among other RNA viruses, demonstrating broad-spectrum effectiveness against these viruses. The cytopathic effect inhibition and virus yield reduction experiments were conducted in a variety of cell lines to evaluate this drug against ZIKV of the African and Asian lineages. A mouse model is used for severe ZIKV infection, which mimics several human illness symptoms such as peripheral viral replication, conjunctivitis, encephalitis, and myelitis, in order to further assess its effectiveness in a pertinent animal model. Viral RNA accumulation measured over time showed strong viral replication in a number of critical tissues, including the brain and testis, where substantial and enduring viral loads were seen. Both immunohistochemical labeling of tissue sections and an infectious culture assay were used to demonstrate the

presence of viral RNA in different tissues. Even when treatment was started when viremia was at its highest, ZIKV-infected mice treated with BCX4430 showed a marked improvement in their general health. The evidence of BCX4430's strong anti-ZIKV action in a deadly mouse model justifies the drug's ongoing clinical research. [1]

Carica papaya fruit

There are various RNA viruses that are common worldwide and are either reemerging or emerging for which there are no approved vaccinations or antiviral medications. A recent example of an emerging virus that has gained international attention due to its link to serious congenital abnormalities and neurological diseases in adults is the Zika virus (ZIKV). Numerous plant extracts high in polyphenols have been utilized as nutraceuticals with strong *in vitro* antiviral properties. In this study, findings show that, without compromising the viability of the cells, papaya pulp isolated from Carica papaya fruit prevents ZIKV infection in human cells. Regardless of the viral strains examined, papaya pulp extract can inhibit the formation of virus offspring in ZIKV-infected human cells by at least 4 logs at non-cytotoxic dosages. To preserve the qualities of papaya pulp throughout time, samples of fermented papaya pulp were tested on ZIKV by lactic fermentation utilizing the bacterial strains Weissella cibaria, Lactobacillus plantarum, and Leuconostoc pseudomesenteroides. It was found that, in a bacterial strain-dependent manner, lactic fermentation of papaya pulp results in a mild reduction of antiviral efficacy in opposition to ZIKV.[2] It was discovered that fermentation produced an IC50 of up to 4 mg/mL, whereas the IC50 of the papaya pulp extract was 0.3 mg/mL. It may be concluded that the fermentation process has a minor impact on the antiviral effect of papaya pulp, which has antiviral activity against ZIKV.

Emodin and Berberine

The Zika virus (ZIKV) has been linked to major health problems, and an intensive quest for new strategies to prevent and treat ZIKV infection is ongoing. Berberine and emodin have a variety of pharmacological effects and have been demonstrated to be very effective against the invasion and replication of various viruses. It was demonstrated that emodin and

berberine have a virucidal effect on ZIKV. Berberine (160 μM) reduced virus infectivity by 77.6%, while emodin (40 μM) reduced it by about 83.3%. Dynamic light scattering data revealed that both drugs greatly reduced the hydrodynamic radius of virus particles in solution. It was found that berberine and emodin, two natural chemicals, have substantial virucidal effects on Zika.[3]

African swine fever virus and its herbal cure

The African swine fever virus (ASFV) kills a significant number of farmed pigs, regardless of age, with a severe and highly contagious hemorrhagic viral illness. Even though the virus poses no threat to people, the current ASFV outbreak may have detrimental effects on the world's ability to secure food supplies. A few antiviral drugs have been discovered in recent research to be able to prevent ASFV infections. Vaccines and antiviral medications are not available at this time, though. Therefore, the search for novel medications to treat ASFV is crucial. We identified novel antiviral medicines using molecular docking and machine learning models based on structural information data on ASFV targets. Using principal component analysis, we verified that molecules exhibiting high affinity inside the region of interest corresponded to subsets within the chemical space. analysis and k-means clustering in FDA-approved medication molecular docking research. Pentagastrin was identified by these techniques as a possible antiviral medication against ASFVs. Lastly, it was also noted that the substance inhibited the activity of AsfvPolX. The current study's findings imply that machine learning models and molecular docking may be crucial in the discovery of possible antiviral medications that combat ASFVs. [4]

The anti-bovine viral diarrhea virus

The anti-bovine viral diarrhea virus (BVDV) activity of several N4-arylsubstituted thiosemicarbazones produced from 1-indanones as well as a group of compounds lacking such substitution in the N4 position of the thiosemicarbazone moiety was synthesized and assessed. of these, derivatives 2 and 15 showed the greatest inhibition of BVDV replication (EC50 = 2.7 ± 0.4 and 0.7 ± 0.1 μM, respectively). Structure-activity relationship (SAR) analysis was used to identify novel critical structural

characteristics associated with the anti-BVDV action. 5,6-dimethoxy-1-indanone (5,6-TSC) thiosemicarbazone was identified as a non-nucleoside inhibitor (NNI) of the BVDV RNA-dependent RNA polymerase in an earlier investigation. Cross-resistance tests were carried out in the current study using the most active substances. These investigations were conducted using BVDV that was 5,6-TSC resistant (BVDV-TSCr T1) and had mutations in its viral polymerase. Compound 15 was equally ineffective against this BVDV mutant. Utilizing MM/PBSA computations and molecular docking investigations, the most potent derivatives at the 5,6-TSC viral polymerase binding site were evaluated. Derivative 15's varying interaction patterns and binding affinities to BVDV-TSCr T1 polymerase and the wild type were important in determining this compound's mode of action.[5]

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CHAPTER 9

MISCELLANEOUS HERBS FOR VIRAL INFECTIONS

DR. SUKIRTI UPADHYAY

Some medicinal herbs such as *Andrographis paniculata*, *Centella asiatica, Curcuma longa, Woodfordia fruticose*, *Phyllanthus emblica*, *Tamarindus indica*, *Terminalia arjuna*, *Azadirachta indica*, *Ferula assafoetida*, *Gymnema sylvestre*, *Gossypium herbaceum*, *Phyllanthus niruri*, *Trachyspermum ammi*, *Withania somnifera*, and *Andrographis paniculate* are also used in traditional system of treatment for curing diseases of viral origin. Nevertheless, very few antiviral drugs have been approved for clinical use, and many viruses are still resistant to effective vaccination. Consequently, it is imperative to create novel antiviral drugs, and natural goods are an excellent place to start.

Some powerful antiviral herbs

Oregano: Popular among the mint family, oregano is prized for its potent therapeutic properties. Carvacrol is one of the plant components that gives it antiviral qualities. Oregano oil and isolated carvacrol both decreased the activity of the murine norovirus (MNV) within 15 minutes of exposure in a test-tube investigation. MNV is the main cause of stomach flu in humans and is extremely contagious. Because human norovirus is known to be difficult to grow in laboratory settings, this virus—which is employed in scientific studies—is highly similar to human norovirus. Additionally, it has been demonstrated that carvacrol and oregano oil have antiviral properties against respiratory syncytial virus (RSV), which causes respiratory infections,

rotavirus, which frequently causes diarrhea in infants and toddlers, and herpes simplex virus type-1 (HSV-1).[1]

Sage: Sage, a fragrant herb and fellow member of the mint family, has long been used in traditional medicine to treat viral infections. The plant's stem and leaves include substances known as sage one and safficinolide, which are primarily responsible for sage's antiviral qualities. According to research conducted in test tubes, this plant may be able to combat HIV-1, the virus that can cause AIDS. Sage extract dramatically reduced HIV activity in one research by keeping the virus from infecting target cells. Numerous forms of basil, such as the holy and sweet kinds, have the potential to combat specific viral diseases.

For instance, a test-tube study discovered that extracts from sweet basil, which included substances like ursolic acid and apigenin, had strong antiviral properties against enterovirus, hepatitis B, and herpes viruses. Tulsi, another name for holy basil, has been shown to boost immunity, which may aid in the fight against viral illnesses. Taking 300 mg of holy basil extract as a supplement dramatically raised the levels of helper T cells and natural killer cells—two immune cells that assist in defending and shielding the body against viral infections—in a 4-week research study involving 24 healthy people.

Fennel: One of the many varieties of the herb fennel plant yields the spice known as fennel seeds. They taste sweet and strong, somewhat like licorice. Italian cuisine has historically made use of fennel seeds. A plant with a licorice flavor, fennel may help combat some infections.Fennel extract shown potent antiviral properties against parainfluenza type-3 (PI-3), which causes respiratory illnesses in cattle, and herpes viruses in a test-tube investigation. Furthermore, the primary ingredient in fennel essential oil, trans-anethole, has shown strong antiviral properties against herpes viruses. Fennel has been shown in animal studies to strengthen immunity and reduce inflammation, both of which may aid in the fight against viral infections.[2]

Garlic: Viral infections are among the many ailments for which garlic is a well-liked natural treatment. Human papillomavirus (HPV)-caused warts in 23 people were studied. After 1-2 weeks, all of the warts in the afflicted

locations were removed by using garlic extract twice a day. Garlic may also have antiviral effects against influenza A and B, HIV, HSV-1, viral pneumonia, and rhinovirus, which causes the common cold, according to earlier test-tube studies. Still, there is a dearth of study to date. Studies on animals and in test tubes show that garlic boosts the immune system's response by promoting immune cells that are protective against viruses.

A multitude of human pathogens, including cancer, are caused by viruses. Viral infections have been linked to several difficult-to-cure conditions and complex syndromes, such as Alzheimer's disease, type 1 diabetes, and hepatocellular carcinoma. Furthermore, epidemic outbreaks brought on by new and re-emerging viruses pose a serious threat to public health due to increased international travel and fast urbanization, especially in the absence of prophylactic vaccinations and antiviral treatments. The recent outbreaks of the West Nile virus, the influenza virus, the measles virus, the dengue virus, and the severe acute respiratory syndrome (SARS) virus are a few examples. However, only a small number of antiviral medications are approved for use in clinical settings, and many viruses are still not effectively immunized against. The matter is additionally worsened by the possibility of drug-resistant mutants arising, particularly in the case of employing inhibitors specific to viral enzymes, which considerably reduces the effectiveness of drugs. Therefore, in the absence of vaccines and conventional medicines, it is imperative to find new antivirals that are both highly efficient and economical for the management and control of viral infections. An abundant source of material for the creation of innovative antiviral drugs is found in herbal remedies and pure natural products. The identification of these natural agents' antiviral mechanisms has provided insight into how they interact with the viral life cycle, including host-specific interactions and viral entrance, replication, assembly, and release. The antiviral activities of several natural products and herbal medicines against many well-known viral pathogens are outlined in this brief report. These pathogens include the coronavirus (CoV), coxsackievirus (CV), dengue virus (DENV), enterovirus 71 (EV71), hepatitis B virus (HBV), hepatitis C virus (HCV), herpes simplex virus, influenza virus, measles virus (MV), and respiratory syncytial virus (RSV).

Glycyrrhiza glabra

Eradicating many viral infections seems challenging because many viruses still lack effective antiviral medications and vaccines. Nevertheless, natural products provide a great source of biodiversity for the development of new structure-activity correlations, innovative antivirals, and efficient treatment and preventive measures against viral infections. Strong antiviral activity has been found in a number of natural products and herbal ingredients, and these findings can aid in the development of derivatives and therapeutic leads (e.g., derivatives of glycyrrhetinic acid as novel anti-HBV agents, derivative of acetoxime from the Mediterranean mollusk Hexaplex trunculus as inhibitor against HSV-1, and derivatives of caffeic acid as a new class of influenza NA antagonist). The finding that punicalagin and chebulagic acid can impede the entry of many viruses by competing with GAG may aid in the development of broad-spectrum antivirals for the prevention and management of numerous viral diseases. Since a lot of the research in this area is still in its early stages, more investigation is recommended to help develop effective antiviral medicines by identifying the bioactive substances, defining the underlying mechanisms, evaluating the efficacy, and considering their potential in vivo applications. Furthermore, as a multi-target therapy may help lower the likelihood of producing drug-resistant viruses, future research should look into the possibilities of combination therapies with other natural medicines or with traditional pharmaceuticals. It is anticipated that natural items will continue to be crucial to the development of antiviral medications.

Terminalia chebula

Chebulinic acid (CA), which was first identified from the floral extract of the Terminalia chebula plant, has been demonstrated to prevent herpes simplex virus-2 (HSV-2) infection, possibly by blocking the viral infection's host entry stage. The action of CA was evaluated against the dengue virus (DENV) and the chikungunya virus (CHIKV), as both viruses rely on receptor glycosaminoglycans (GAG) for host entrance, similar to HSV-2. When 8 μM CA and DENV-2 were co-treated, the virus titer at 120 hours after infection decreased by 2 logs, to 4.0 log10FFU/mL, from 5.95 log10FFU/mL in the virus control. On the other hand, under all

circumstances, there was no inhibitory impact of CA on CHIKV infection. CA's mode of action was studied in silico using the envelope glycoproteins of CHIKV and DENV-2. In the process of docking, CA showed similar binding at several places on the DENV-2 envelope protein, including the GAG binding site, which is important for host attachment and fusion in the past. This suggests that these sites are blocked. On the other hand, CHIKV envelope protein-2's GAG binding site was not bound by CA. Based on the results of the in vitro and in silico studies, CA has the potential to be developed as a therapeutic agent against DENV-2 infection since it can suppress the virus at the entry stage of its infection cycle.[3]

- **Antiviral herbs:** One of the most traditional and effective natural virus destroyers, antiviral herbs are covered in greater detail in the section below.
- **Specific foods**: Some foods, like onions, garlic, and mushrooms, naturally contain antiviral qualities, as we covered in our guide to foods that improve immunity.
- **Infrared sauna**s: These are saunas that employ light waves from infrared lamps to heat your body internally, as opposed to warming the air around you. Some claim that raising your body temperature helps your immune system by killing viruses and other infections as well as promoting the formation of white blood cells. Just like when your body naturally tries to fight off a sickness by raising a fever. While there's still not a lot known about using infrared saunas to kill viruses, there's a growing body of research on their general health benefits, and there are no known negative side effects, so it’s worth a try!
- **UV light**: Studies have demonstrated the ability of minimal, human-safe UV light to destroy airborne viruses. Purchasing a UV sanitizer is a more sensible option as most of us won't be flooding our houses with UV light, and it may be used to eradicate any viruses that might be present on surfaces.
- ***Colloidal silver***: When administered topically, colloidal silver, or microscopic silver particles suspended in liquid, has long been promoted as a natural virus killer. According to studies, silver can destroy viral compounds. However, overuse of silver can result in

agyria, a condition in which you physically turn silver (well, blue-gray).[4]

- **Ozone** is an energy-rich, naturally occurring molecule with special physiochemical and biological characteristics. By oxidizing the virally invaded cells and expelling them from our bodies, ozone therapy disrupts the reproductive cycle and destroys the viral DNA, which is then replaced by healthy cells. Promising research has been done on how ozone can boost the immune system and inactivate viruses to hasten healing. Ozone generators will come with detailed instructions on how to correctly administer the gas, which is crucial because it cannot be inhaled. Additionally, there are potential adverse effects, such as viruses dying off, which frequently make patients feel worse before getting better. [5]
- **Basil**: It's true that this staple of Italian cooking doubles as an antiviral herb. In one study, the most popular kind of basil, sweet basil, was shown to have strong antiviral properties against a range of viruses. In another study, the levels of cells in basil supplements were found to be much higher, indicating that the supplement is helping the body fight against viral infections.[6]
- **Elderberry/Sambucas**: Sambucas are a family of plants, and the elderberry is the most popular variety. Elderberries are also a potent herbal remedy with antiviral properties. According to studies, elderberry juice boosts the immune system, eradicates influenza, sometimes known as the flu virus, and may even offer protection against HIV/AIDS and herpes. Furthermore, research indicates that it significantly lessens upper respiratory tract symptoms brought on by viral infections, which is very pertinent in light of COVID-19 symptoms. [7]
- **Echinacea**: One of the most well-known plants for antiviral properties, echinacea is typically found in capsule form. Research indicates that it provides a boost to your immune system and may be useful in warding off certain viruses, such as the flu and herpes.[8]
- **Fennel:** Known for its licorice flavor, fennel is a potent herb that fights viruses. In addition to potentially enhancing immune response and lowering inflammation, it has a potent inhibitory effect on herpes and other respiratory viruses.[2]

- **Oregano**: Another popular and simple herb for antivirals. In just fifteen minutes, a test-tube study demonstrated that oregano could suppress viral activity. Different studies have discovered that oregano oil is helpful against a variety of different viruses, including those that cause respiratory illnesses.[1]
- **Pau D'Arco**: The bark of the Amazon tree is said to be able to treat a variety of infections. By destroying the DNA and RNA (genetic material) contained in the viral protein, it stops virus cells from penetrating human cells and proliferating.
- **Peppermint**: In a single study, peppermint leaf extract considerably decreased a respiratory virus's viral activity while also reducing inflammation. Additionally, chemicals in peppermint tea have inherent antiviral and anti-inflammatory properties.
- **St. John's Wort**: Known for its antiviral properties, St. John's Wort includes compounds called hypericin and pseudohypericin that combat viruses that mimic human cells.

You have a wide range of choices for antiviral herbs. There are several approaches to take. Viral respiratory infections (VRI) have long been treated and prevented using some antiviral herbal medications. An overview of these herbs is given here. There is extensive discussion of the advantages and consequences of a variety of antiviral herbs. Because the majority of these herbs naturally stimulate the immune system and reduce inflammation, they can help prevent an overreaction of the immune system (a "cytokine storm") to virtual reality illnesses while also enhancing the immune system's ability to fight off infections. These claims are supported by scientific evidence, which is discussed. Reviewing the shortcomings of studies on *Echinacea angustifolia* (narrow-leaved purple coneflower), especially those that employed much too low dosages A discussion of the evidence supporting the prevention of VRI by several herbs, including *Panax ginseng* (Asian red ginseng), *Panax quinquefolius* (American ginseng), Camellia sinensis (green tea), and *Allium sativum* (garlic), follows the presentation of a customized method to formulation for VRI patients. [85]

Respiratory viral infections (VRI) remain one of the most prevalent diseases in humans. Patients suffering from influenza, viral pharyngitis, acute bronchitis, and the common cold can benefit greatly from herbal treatment.

Although influenza vaccinations are readily available and annually advised, their population acceptance is very low, and their efficiency varies (based on factors such as viral mutation during manufacture, strain matching accuracy, and other factors). Furthermore, other viruses are unaffected by this vaccination. The symptoms of colds and influenza are only temporarily relieved by conventional therapies, which are frequently ineffective in this regard (as nonsteroidal anti-inflammatory medicines are). The availability of conventional medications that specifically target these viruses is limited, and even when they do, the side effects of neuraminidase inhibitors (oseltamivir, zanamivir) for influenza are severe and the efficacy is just mediocre.

Herbal remedies are still quite effective in treating and preventing VRI. This article will first discuss the use of herbs to treat certain infections, covering both conventional and scientifically studied remedies. Next, research-based prophylactic strategies will be spoken about. These steps are especially crucial to giving medical professionals evidence-based substitutes for antibiotics, which are inappropriate for treating solely viral infections.

Questionable herbs

The National Institutes of Health (NIH) states on its website: The media has reported that some people are pursuing "alternative" treatments to either treat or prevent COVID-19 infection. Herbal treatments and teas are a few of these alleged cures

Oregano

"At this time, there is no vaccine available to prevent norovirus," said the U.S. Centers for Disease Control and Prevention (CDC). Although oregano oil is antimicrobial, "there's no evidence it can [kill norovirus] inside your body," according to a 2014 podcast by the popular scientific magazine Scientific American, as "it works to inactivate pathogens...before they get inside." The CDC states that while rotavirus vaccinations "are very effective"

at preventing infection, there is no specific medication to treat rotavirus. The CDC notes that while there is no known cure for RSV, "most RSV infections go away on their own in a week or two" and that over-the-counter fever decreases and pain relievers, such as acetaminophen or ibuprofen, can be used to control fever and discomfort.

Licorice

Selecting an HIV regimen is the first step in HIV treatment, commonly known as antiretroviral therapy, or ART, according to the NIH. HIV medications are taken daily by people on antiretroviral therapy (ART).ART lowers the risk of HIV transmission and prolongs the healthy, longer lives of those living with the virus. Over thirty HIV medications have been licensed by the US Food and Drug Administration (FDA) to treat HIV infection.

According to Johns Hopkins Medicine, "antiviral oral medication" is the most effective treatment for oral herpes, also referred to as herpes simplex 1 (HSV-1). As for herpes simplex 2 (HSV-2) or vaginal herpes, the CDC says that while there is no known cure, antiviral medications can "prevent or shorten breakouts during the period the person receives the medication."

The virus that causes severe acute respiratory syndrome (SARS) is called SARS-associated coronavirus (SARS-CoV), according to the Centers for Disease Control and Prevention (CDC). It is not to be confused with SARS-CoV-2, the coronavirus that triggers COVID-19. It is stated by the CDC that "SARS-CoV is being tested with various antiviral drugs to see if a successful therapy can be found," even though there is now "no known SARS transmission anywhere in the world."

Holy basil

According to the post, holy basil can boost immunity and treat hepatitis B, enterovirus, and herpes infections. According to WebMD, holy basil does not yet have enough data to support its use in treating viral hepatitis or other illnesses. On the other hand, the CDC states that a Hepatitis B vaccine "is offered to all age groups to avoid HBV infection." Specifically, the CDC states that there is no known treatment for enterovirus infections.

Garlic

According to the post, garlic can treat viral pneumonia, herpes simplex type 1 (HSV-1), HIV, human papillomavirus (HPV), influenza A and B, and rhinovirus, the common cold's responsible. The National Institutes of Health states that "a great deal of research has been conducted on garlic, but much of it involves small, preliminary, or low-quality studies."

The CDC notes that "HPV infections and cervical precancers (abnormal cells on the cervix that may result in cancer) have decreased significantly since the vaccine has been in use" and recommends HPV immunization "for everyone over the age of 26, if not already vaccinated." The CDC claims that "different types (A & B) and subtypes (influenza A) of influenza circulate and cause disease over the course of a flu season." The best approach to helping prevent against flu is to get the annual flu vaccine, according to the CDC.

According to the CDC, vaccines for pneumonia that are now available in the United States can aid in defending the body against some of the bacteria and viruses that cause the illness. These comprise the vaccinations against measles, pertussis (whooping cough), varicella (chickenpox), influenza (flu), and Haemophilus influenzae type b (Hib). The common cold, which is brought on by rhinoviruses, cannot be prevented by vaccination, according to the CDC. The National Institutes of Health states that there is "not enough evidence to show whether garlic is helpful for the common cold" in terms of symptom relief or accelerating healing.

Ginger

The article states that avian influenza (bird flu), RSV, and feline calicivirus (FCV) can all be treated with ginger. There is some data about ginger's application in alleviating nausea and vomiting in humans, according to the NIH. It is significantly less known how beneficial ginger is for different medical conditions.

Avoiding exposure sources is the best way to prevent infection with avian influenza A viruses, according to the CDC. Although there is currently no treatment for feline coronavirus (FCV), Cornell University College of

Veterinary Medicine states that pet owners can give their cat supportive care while its immune system is being strengthened.

Fennel

According to the report, fennel boosts the immune system, decreases inflammation, and treats HPIV-3 and herpes viruses. As of right now, "no vaccine that safeguards you against infection brought about by human parainfluenza viruses (HPIV)" exists, according to the CDC. To reduce the risk of catching HPIV, the CDC advises staying away from touching the mouth, nose, or eyes, washing your hands often with soap and water for at least 20 seconds, and preventing close contact with ill people. According to WebMD, there is "insufficient evidence" that fennel helps to heal colitis, airway edema, bloating, and other illnesses.

Lemon balm

According to the article, lemon balm may cure enterovirus, herpes, HIV, and avian flu. WebMD notes that for herpes simplex 1, "applying a lip balm, including a lemon balm, to cold sores (LomaHerpan by Infectopharm) appears to shorten healing time and decrease symptoms if applied at the early stages of infection," even though the treatments for these conditions have been discussed previously in this article.

Elderberry

Elderberry is said to treat "flu and common cold, influenza virus, and upper respiratory viral infections." The common cold is associated with an upper respiratory viral illness, much as influenza virus is synonymous with flu.

Oral administration of elderberry juice syrup within 48 hours of the onset of symptoms, as reported by WebMD, "seems to ease flu symptoms while minimizing the length of time the flu lasts." It also says that "it does seem to decrease the course of colds and reduce cold symptoms," even though there is "insufficient evidence" in favor of its use not treating anything other than the common cold.

Peppermint

According to the post, peppermint can "significantly decrease levels of inflammatory compounds" and is used to treat RSV. "A small amount of research has been conducted on peppermint oil, primarily focusing on IBS," according to the NIH. Nevertheless, there is "not enough evidence to show whether peppermint leaf is helpful for any condition," and "very little research has been done on peppermint leaf."

Rosemary

The article claims that rosemary helps treat herpes, HIV, hepatitis, and influenza. While rosemary may help with memory enhancement, WebMD states that there is "insufficient evidence" to support its usage, not treating any specific ailments.

Echinacea

The article adds that echinacea, which is typed wrongly as "enchnia," can be "used for the treatment of an extensive variety of conditions, including viral infections." The National Institutes of Health claims that while "many studies have been done on echinacea and the common cold," "taking echinacea after you catch a cold does not appear to shorten the time that you'll be sick." Furthermore, although "taking echinacea while you're well might decrease your chances of developing a cold," the NIH states that the research "isn't completely certain."

Proven herbs with Antiviral activity

Since coronaviruses have few recognized treatments, the SARS-CoV2 outbreak resulted in catastrophic occurrences. As a result, there is a global need to look for agents that can combat SARS-CoV2 to strengthen human immunity during COVID-19. The Ministry of AYUSH of India recommends using cooking spices like turmeric, cumin, coriander, and garlic as part of Ayurveda's immunity-promoting strategies for self-care during the COVID-19 pandemic. Additionally, they suggested drinking kadha, a herbal tea/decoction made of basil, cinnamon, black pepper, ginger, and raisins, once or twice a day. You can add lemon juice or pure

sugar to enhance the flavor. You can take 150 mL of heated milk (Golden Milk) once or twice a day with a half teaspoon of turmeric powder added. Together with a survey-based analysis, this article provides an overview of the scientific research on the antiviral properties of spices and herbs, as well as their derivatives, mechanisms of action, and future research opportunities.

Many therapeutic plants and herbs, such as *Allium sativum* (garlic), *Tinospora cordifolia* (giloy), *Ocimum basilicum* (tulsi), and others, are recognized as immune-stimulating agents. In addition to their antiviral qualities, some spices, including clove, cinnamon, ginger, black pepper, and turmeric, are known to strengthen immunity.

Curcuma longa L. (turmeric)

Throughout its natural habitat, turmeric (*Curcuma longa* L.), which is a member of the ginger family (Zingiberaceae), grows throughout Southeast Asia and India. This plant's rhizomes are rich in secondary metabolites, with curcuminoids, sesquiterpenes, steroids, and polyphenol serving as the main bioactive compounds. Turmeric (Curcuma longa) contains curcumin, a naturally occurring polyphenol that has been used for ages in traditional Asian medicine to treat a variety of ailments. Numerous studies have demonstrated that curcumin has some pharmacological qualities like anti-inflammatory, anti-angiogenic, and anti-neoplastic capabilities without being harmful. According to the Food and Drug Administration (FDA), it is "Generally Recognized as Safe." A dose of up to 12 g/day of curcumin was found during the clinical studies to be risk-free and to have no adverse effects when consumed by humans. Curcumin's efficacy against a variety of viruses has been noted, including those that cause hepatitis, SARS coronavirus, influenza, HIV, herpes simplex, dengue, chikungunya, and other viruses. Curcumin's capacity to control a variety of molecular targets that support a range of cellular processes, including transcription regulation and the activation of cellular signaling pathways, is a further indication of its antiviral properties.[9]

Zingiber officinale (ginger)

One of the significant medicinal plants that grows naturally in many different nations is ginger. Ginger, Zingiber officinale, belongs to the family

Zingiberaceae, and the other renowned members of this plant family include turmeric, cardamom, and galangal. The plant is native to Southeast Asia and is grown throughout the region, especially in India.

The bioactive substances found in ginger, such as phenolic groups, alkaloids, and steroids, are abundant and offer therapeutic benefits. The zingiberol, as well as its counterparts shogoals, paradol, and zingerone, is the main aromatic component of the rhizome. In addition to the main bioactive components, the subcompounds 4gingerol, 6gingerol, 8gingerol, 10gingerol, 6shogaols, and 14shogaols have been demonstrated to possess antiemetic, antipyretic, analgesic, antiarthritic, and anti-inflammatory qualities.

Numerous studies have demonstrated the efficacious antiviral action of ginger and its bioactive components against a variety of viruses, including SARS-CoV-2, influenza, herpes simplex, human respiratory syncytial virus, chikungunya virus, and others.[10]

***Cinnamomum cassia* (cinnamon)**

One species of aromatic tree in the *Lauraceae* family is *Cinnamomum cassia*. For a very long time, traditional Chinese, Indian, Persian, and Unani medicines have made extensive use of cinnamon. For thousands of years, people have utilized cinnamon as a popular spice in many nations. The bark of the young branches of this plant yields cinnamon, which is used as a daily condiment throughout the world. It has great economic value and can also be utilized as a material for medicinal items. It is used to treat several illnesses, including headaches, fever, leukorrhea, amenorrhea, diarrhea, and flatulence. Additionally, it has been shown that using cinnamon daily helps prevent throat infections.

The antibacterial properties of 21 chemical components found in cinnamon bark, including cinnamaldehyde (60.41%) and eugenol (3.19%), are present. Cinnamon has been found to have antibacterial, antiviral, antifungal, antioxidant, antidiabetic, anticancer, gastroprotective, and immunomodulatory properties. A study found that cinnamon's low dose (10 mg/kg) merely increased serum immunoglobulin levels, whereas a greater dose (100 mg/kg) markedly enhanced the phagocytic index, serum immunoglobulin

levels, and antibody titer. Thus, whereas the low dose only had an impact on humoral immunity, the greater amount improved both cell-mediated and humoral immunity. Researchers Moattari, Lavaee, Rastegarfar, and Moshaverinia examined the impact of a hydroalcoholic cinnamon extract on the herpes simplex virus-1. They discovered that by preventing viral attachment to cells, the hydroalcoholic extract of cinnamon was efficient in lowering the viral titer of HSV-1.[11]

***Syzygium aromaticum* (clove)**

Because of its antibacterial properties against oral germs, clove (Syzygium aromaticum), a member of the Myrtaceae family, is used in medicine all over the world as an antiseptic against infectious infections. Due to its antibacterial properties, clove is frequently utilized in the food industry to extend shelf life. Clove buds, clove oil, eugenol, and oleoresins are safe to use as food supplements, according to the FDA.

Flavonoids, hydroxycinnamic acids, hydroxybenzoic acids, and hydroxiphenylpropens are some of the primary phenolic chemicals found in clove. Eugenol is the primary bioactive ingredient in cloves. Eugenol demonstrates extensive antibacterial properties against fungus, bacteria, and acid-fact bacteria (Gram-negative). The well-known antiemetic (relieves nausea and vomiting) and carminative qualities of cloves are also widely recognized. At a dosage of 5 µg/mL, eugeniin—a substance extracted from the herbal extracts of *S. aromaticum* and *Geum japonicum*—was found to be anti-Herpes Simplex Virus. Eugenol inhibits viral replication and lowers infection, whereas Eugeniin acts as a specific inhibitor of HSV-1 DNA polymerase to prevent the synthesis of viral DNA.[12]

***Piper nigrum* (black pepper)**

Due to its strong aroma, piper, a member of the Piperaceae family, is known as the king of spices. Many tropical countries including Brazil, Indonesia, and India cultivate black pepper. Significant biological qualities of piper nigrum make its bioactive components useful in fragrance, medicine, and food preservation. Ayurveda, Siddha, Unani, and Tibetan traditional medicine all make extensive use of piperine, a potent alkaloid found in black pepper. It contains the potent alkaloid piperine (1-peperoyl piperidine),

which has several noteworthy pharmacological properties, including those that are antihypertensive, anti-Alzheimer's, antidepressant, anti-platelet, anti-inflammatory, antioxidant, antipyretic, anti-tumor, anti-asthmatic, analgesic, and antimicrobial and antiviral.[13]

***Ocimum basilicum* L. (basil)**[14]

2. The results reveal that crude aqueous and ethanolic extracts of OB and selected purified components, notably apigenin, linalool, and ursolic acid, have a wide range of antiviral activity. Ursolic acid had the highest activity against HSV-1 (EC50 = 6.6 mg/L; SI = 15.2), ADV-8 (EC50 = 4.2 mg/L; SI = 23.8), CVB1 (EC50 = 0.4 mg/L; SI = 251.3), and EV71 (EC50 = 0.5 mg/L; SI = 201), while apigenin had the highest activity against HSV-2 (EC50 = 9.7 mg/L; SI = 6.2), ADV-3 (EC50 = 11.1 mg/L; SI = 5.4)[14]

Ocimum basilicum L. (OB), popularly known as sweet basil, is a well-known medicinal herb from the Labiatae family. For many years, food, cosmetics, dental, and oral products have all made substantial use of the essential oils of these plant materials. According to numerous research, basil is a natural spice with antibacterial properties. Numerous bacteria, fungi, and parasites have been documented to be resistant to the essential oils of OB. Treatments for conditions such viral ocular, respiratory, and hepatic infections involve the various OB components. Sesquiterpenoids (caryophyllene and farnesol), triterpenoids (ursolic acid), and monoterpenoids (carvone, cineole, fenchone, geraniol, linalool, myrcene, and thujone) have all been reported to be present in ocimum basilicum.and flavonoid (apigenin)

Multiple research studies have shown that the aqueous and methanol extract of basil leaf and seed oil increases the number of lymphocytes, phagocytic activity, T-helper and natural killer cells, neutrophil count, antibody titer, and other defense mechanisms, thereby improving the immune response against a variety of infections. Human immunodeficiency virus (HIV) and herpes simplex virus (HSV-1) infections are both inhibited by ursolic acid, according to observations.[15]

Allium sativum L. (garlic)

The *Liliaceae* family, which includes the garlic plant *Allium sativum* L., is native to Asia, although it is widely grown in China, North Africa (Egypt), Europe, and Mexico. It has been utilized for thousands of years as a medication. This plant is a bulb that can grow to be 25–70 cm tall, and its blossoms are used to flavor and spice cuisine. Garlic has a high nutritional content, enhances food flavor, and relieves dyspepsia. Numerous pharmacological benefits of garlic, including anthelmintics, anti-inflammatory agents, antioxidants, and antifungals, are associated with low toxicity.[16]

***Azadirachta indica* (neem)**

Azadirachta indica, the scientific name for the neem tree, is an evergreen plant with a rapid growth rate that is a member of the Meliaceae family. Herpes simplex virus type 1 (HSV-1) causes a wide range of health concerns, including skin and ocular ulcers as well as encephalitis. We show that an aqueous extract prepared from the bark of the neem plant Azardirachta indica is a strong inhibitor of HSV-1 entrance into natural target cells. Neem bark extract (NBE) inhibited HSV-1 entrance into cells at doses ranging from 50 to 100 μg/ml.[17]

***Tinospora cordifolia* (giloy)**

Secondary metabolites obtained from *Tinospora cordifolia* showed an excellent antiviral approach as compared to standard drugs for SARS infection in molecular docking studies; it targets the SARS-CoV-2 main protease Out of five standard drug molecules, two widely used antiviral drugs (Favipiravir and Remdesivir) are ascribed as the most potent molecules based on their highest docking score in the present study. Columbin, Tinosporide, N-trans-feruloyl-tyramine-diacetate, Amritoside C, Amritoside B, Amritoside A, Tinocordifolin, Palmatoside G, Palmatoside F, and Maslinic acids are other molecules considered to be the key molecules based on their docking score (range between -5.02 to −5.72).[18]

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CHAPTER 10

FROZEN VIRUSES: NEW THREATS

DR. SUKIRTI UPADHYAY

Ancient bacteria live in freezing Arctic soils and riverbeds. Bacteria and viruses from thousands of years ago are preserved within prehistoric layers of permafrost.

Warming temperatures could cause most of the ice to melt, freeing these bacteria from their frozen cages. Once unleashed, undiscovered pathogens may infect people or other animals.

"The risk is bound to increase in the context of global warming, in which permafrost thawing will continue to accelerate and more people will populate the Arctic," says Jean-Michel Claverie, a computational biologist at Aix-Marseille University in France who studies ancient and exotic So far, scientists have only researched permafrost viruses that infect single-celled animals known as amoebas because they are harmless and serve as a good model for others that may be lurking beneath the ice.

Zombie virus

"We will never risk isolating a virus that is eventually capable of infecting modern mammals," Jean-Michel Claverie told Live Science via email. "We don't have formal proof that viruses other than amoeba-specific viruses might survive as long, but there's no reason why they couldn't because all viruses have the same property: they're inactive particles outside their host cells. We do not want to incur the enormous danger of causing a new

pandemic with unknown 'zombie' viruses from the distant past only to prove that we are correct."

Here are eight viruses that scientists have recovered from permafrost, ranging from germs resurrected from clumps of mammoth wool to particles hidden in a Siberian wolf's petrified guts.

The deadliest viruses in history

1. *Pithovirus sibericum*

Pithosvirus sibericum is one of the largest viruses ever discovered, with a cork-like structure Pithovirus sibericum is one of the largest viruses ever discovered. It is around 1.5 micrometers long, the size of a microscopic bacterium, and belongs to a group known as "giant viruses," which are double-stranded DNA viruses that are visible under a light microscope (with some exceptions). P. sibericum resembles a thick-walled oval with an opening at one end, topped with a cork structure and a honeycomb-like grid.

Scientists hunting for unknown pathogens discovered *P. sibericum* nestled deep inside a core of ancient Siberian permafrost that was extracted in 2000 from Kolyma, in the Russian Far East. They resurrected the 30,000-year-old virus by exposing a permafrost sample to amoebas, which are the only known *P. sibericum* hosts. (The virus is harmless to humans and other animals.) The researchers named the virus after the Greek word "pithos," which refers to large containers, or amphoras, used by the ancient Greeks to store wine and food. They published their results in a 2014 study in the Proceedings of the National Academy of Sciences.

2. *Mollivirus sibericum*

Mollivirus sibericum was discovered frozen in the same 30,000-year-old Siberian permafrost sample as *P. sibericum , M. sibericum* particles are smaller than those of P. sibericum (0.6 to 1.5 micrometers in length), yet they are still visible under a light microscope and qualify as large viruses. The approximately spherical virus is encased in a hairy protective covering and can create and release 200 to 300 new viral particles for each amoeba it infects.

Although *M. sibericum* is not harmful to people or other animals, the discovery of two ancient viruses in a single sample implies that dormant diseases may frequently dwell under permafrost, researchers noted in a 2015 study published in the journal Proceedings of the National Academy of Sciences.

3. Pithovirus mammoth

Pithovirus mammoth, *Pandoravirus mammoth* and *Megavirus mammoth* were discovered in a single, 27,000-year-old permafrost sample containing mammoth wool.

Pithovirus mammoth is the second strain of Pithovirus ever discovered, and it was identified from a clump of 27,000-year-old petrified mammoth wool discovered on the banks of the Yana River in the Russian Far East. P. mammoth possesses a huge and elongated particle measuring 1.8 micrometers in length, with a cork-like structure comparable to P. sibericum. Claverie and his colleagues described P. gigantic in a paper published earlier this year. That study revealed 13 "zombie" viruses recovered from Siberian permafrost, three of which—P. mammoth, Megavirus mammoth, and Pandoravirus mammoth—were discovered in the same archaic sample.

4. Pandoravirus mammoth

P. mammoth is a member of the Pandoraviridae virus family, which includes the great majority of viruses recovered from permafrost. Pandoraviruses are gigantic viruses that infect amoebas and feature massive, amphora-shaped particles that can be up to 1.2 micrometers long.

P. mammoth was discovered in a 27,000-year-old frozen sample of mammoth wool from the Yana riverbank, as well as the 28,600-year-old petrified content of a mammoth's stomach in the Lyakhovsky Islands off the coast of northeastern Russia.

The team tested the newly discovered Pandoravirus strain on amoebas as well as human and mouse cells, as is routine procedure to ensure that viruses cannot infect mammalian cells.

5. Pandora virus

Pandoravirus yedoma is the oldest virus recovered from permafrost to date. Researchers identified the 48,500-year-old disease that infects amoebas in frozen deposits beneath a lake in Yukechi Alas, Russian Far East. *P. yedoma* is one of 13 "zombie" viruses reported in a study.[1]

Researchers utilize radiocarbon to date viruses trapped in permafrost, which is a radioactive kind of carbon that decays at a predetermined pace and can aid in determining the age of biological material. However, in samples older than 50,000 years, the remaining radioactive carbon is so tiny that existing dating methods cannot reliably date the material.

6. Megavirus mammoth

Megavirus mammoth is the first virus from the Mimiviridae family to be identified in permafrost. Mimiviruses were the first viruses recognized as gigantic viruses by researchers after being discovered in the water of a cooling tower in Bradford, England, in 1992. Mimiviruses infect amoebas and have particles measuring 0.5 micrometers in diameter and wrapped in a capsule with 20 identical, triangular faces. Megaviruses, including M. mammoth, are members of the Mimiviridae subfamily and have similar traits. Researchers identified the unique strain from a 27,000-year-old clump of ice and mammoth wool unearthed on the Yana riverside, along with P. mammoth.

7. Pacmanvirus lupus

Pacmanviruses are a newly discovered category of amoeba-infecting viruses that are distantly linked to the African swine fever virus from the Asfarviridae family. Scientists named them after the video game "Pac-Man" because, when shattered, the protein shell resembles an open mouth.

Pacmanvirus lupus is the group's third recorded member and the first strain found in permafrost, especially in the frozen intestinal remnants of a Siberian wolf (Canis lupus) that died 27,000 years ago. Pacmanviruses are categorized as enormous viruses, but the new strain is only 0.2 micrometers long and invisible under a light microscope.

8. Cedratvirus lena

Cedratviruses are gigantic viruses that infect amoebas and are part of the Pithovirus family, which also includes P. sibericum and P. mammoth. Scientists discovered three previously unknown strains of Cedratvirus in various areas in the Russian Far East.

Researchers collected Cedratvirus lena from permafrost on the muddy banks of the Lena River in Russia's Far East. The novel strain has an elongated particle measuring 1.5 micrometers in length, similar to P. sibericum, but with two cork-like structures at each end rather than one.[2]

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CHAPTER 11

CONCLUSION

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It is very hard to write down the conclusion of this book, as many viral diseases are discussed, along with their herbal treatments, limitations, and comparisons with Vaccines. Recently more scientists have been inclined toward plant extract and secondary metabolites of plants for conducting antiviral studies. Molecular docking is an important tool for predicting the antiviral properties of phytoconstituents. In India, there are many examples in Ayurvedic texts that uncurable diseases, genetic disorders, and diseases of unknown origin can be cured by ancient sages using herbs and their decoctions, etc. So, in the present era, we found that those claims were true and validated through *in vitro, in vivo*, and *in silico* studies.

For antiviral effects, vaccines may be more potent but they have some serious side effects and are not suitable for every person and some vaccines are very expensive too. Our earth has a rich heritage of different geographical areas and herbs, maybe they have genome-forming effects so they can combat the effect of genetic material called viruses or virus particles, as in nature many genetic diseases are recessive so potent and effective herbal extracts may be answered to these deadly viral infections which make the body susceptible to multiorgan failure.

I recommend the use of herbs and herbal extracts in daily life for enhancing immunity and fighting infectious diseases, but herbs may be free of toxicity and adulteration.