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Review Article

A COMPREHENSIVE STUDY OF RECENT BREAKTHROUGHS IN THE MANAGEMENT OF DYNAMIC VIRAL INFECTIONS

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ABSTRACT

Infectious diseases have been known to human civilization since the dawn of humanity. Infectious disorders are caused by various microorganisms (bacteria, fungi, and viruses). Viruses are the most well-known of all microbes. Viruses are the most well-known type of microbe. They are ultramicroscopic intracellular parasites that require a host cell to survive and reproduce. Viruses have either DNA or RNA as genetic material and have been linked to various diseases in humans, animals, and plants. The war between viruses and humans is ongoing, as both will employ diverse ways to oppose each other. Antiviral treatment and improved technology development a time-consuming process. Despite advanced instruments and tight quality control systems, only a few numbers of antiviral medications or treatment technologies are approved for human use. The cause could be side effects or antiviral medication resistance. Increased understanding of viruses, their infection mechanisms, and the rapid evolution of novel antiviral methods and methodologies will accelerate the creation of novel antiviral medications. This review focuses on the worldwide picture of drug discovery for infectious diseases and contemporary improved methodologies and antiviral therapy options.

Keywords: Virus, Infections, Novel technologies, Resistance, Pandemic, Virology

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INTRODUCTION

Economic integration, industrialization, urbanization, and mass migration are all intricately linked, rendering today's globe laden with a range of public health dangers associated with viral infections [1]. The emergence of new viral infectious illnesses, the persistence of previously studied infectious diseases, and the rise in antibiotic resistance of pathogenic microbes have all posed severe threats to human health. Understanding the regional and temporal prevalence of infectious diseases is a difficult undertaking. More than ten large viral disease epidemics or pandemics in human populations have occurred in the last two decades, caused by coronavirus, alphavirus, myxovirus, filovirus, norovirus, and flavivirus family members. Furthermore, henipaviruses, bunyaviruses, arenaviruses, and other zoonotic RNA viruses have caused modest, occasional epidemics [2].

Forecasting future outbreaks is difficult, as pre-epidemic forms persist in reservoirs and sporadically spread to humans and animals [3]. Some viruses can sustain many types of persistent infection in distinct cells at the same time. The cell type and physiologic condition of the cell may or may not influence the type of chronic infection. Epstein-Barr virus (EBV), for example, latently infects B cells but is discharged for extended periods from productively infected pharyngeal epithelial cells (chronic infection). As a result, persistent infection with the same virus may entail numerous types of persistence in one human, each of which might grow more or less essential as the individual reacts to the disease. This study was conducted to provide insight into current trends for managing common viral infections [4].

Evolution and adaptation to human host

As a result, prolonged infection with the same virus may result in multiple types of persistence in one person, each of which may become more or less important as the individual reacts to the sickness. This document was created to assist you in understanding the most recent developments in the treatment of the most prevalent viral infections [4]. Viral genetic changes, re-assortment, or virus-host genetic recombination may result in the development of stable virus descendants in human populations during the human adaptation process. As a result, such human-adapted viruses may circulate asymptomatically and go undiscovered until their novel clinical symptoms are discovered.

A recently isolated HEV genotype 3 from a chronic hepatitis E patient with a recombinant virus-host RNA genome was demonstrated to infect cultured human, pig, and deer hepatocytes [7]. It is assumed that there is a reservoir of human virus species that has yet to be uncovered. The composition of such a viral pool is dynamic, changing over time; for example, while some virus species fall extinct in their natural hosts, others continue to evolve. More typically, new species emerge as a result of species-crossing jumps from one host to another [8]. Humans are thus merely "incidental" or "spillover" hosts for viruses. In the absence of a reservoir, only a small number of such viruses can remain in specific human groups (endemics) or spread across populations (epidemics). Differential host characteristics such as age, health, physiology, nutritional state, exposure history, concurrent infection with more than one pathogen, immune competence, and heredity all influence human susceptibility to infection. As a result, breakthrough tools for diagnosing and treating the most potent viral infections are required [9, 10].

Epidemiology

Since ancient times, the emergence of new and/or re-emerging pathogens has had a profound impact on human health. The "Spanish flu," which killed tens of millions in the early twentieth century, was the most destructive natural disaster in human history [11]. The flu pandemic resurfaced in 1957 as "Asian flu" and later in 1968 as "Hong Kong flu," killing approximately three million people [12].

The finding of the human immunodeficiency virus (HIV) in the first decade of the 1980s sparked global interest in emerging novel viral diseases and research. New outbreaks of infections have resulted in the discovery of a varied array of extremely deadly viruses, primarily those belonging to the Filoviridae, Arenaviridae, Bunyaviridae, Paramyxoviridae, Coronaviridae, Flaviviridae, Togaviridae, and Hepeviridae families [13]. BK virus (BKV), JC virus (JCV), Merkel cell polyomavirus (MCV or MCPyV), severe fever with thrombocytopenia syndrome virus (SFTSV), Hantavirus (HTNV), and Sin Nombre virus (SNV) are only a few examples [14-18]. Following the fatal instances of Lujo virus in southern Africa in 2008, another virus, Lassa virus (LASV), first described in Nigeria in 1969, re-emerged in 2009 in Guinea, Liberia, and Mali, in Ghana in 2011, and in Benin in 2014 [19, 20].

Human metapneumovirus (hMPV) was discovered in the Netherlands in 2001 and was later related to an acute lower respiratory tract infection in infants, much like respiratory syncytial virus (RSV). In 2013, a novel avian influenza A strain (H7N9) of "bird flu" was detected in China, as well as the Middle-East respiratory sickness (MERS)-CoV [21]. Notably, whereas 2015 was plagued by the recurrence of the Ebola virus, 2015/2016 has seen an outbreak of the Zika virus (ZIKV) [10, 20]. Despite significant advances in pathogen biology, advancements in prevention, and their impact on public health and the worldwide economy, the origin of emerging pandemic viruses remains a mystery.

In Wuhan, China, December 2019 has been recognized as a historic month for the onset of the coronavirus disease, often known as viral pneumonia. This outbreak has spread to around 220 nations, with more than 180,906,466 confirmed cases, 3,919,082 confirmed deaths, and 165,531,010 recovered cases worldwide till June 25, 2021 [22]. The most recent viral infections include RHDV2, a highly contagious fatal disease in rabbits (July 2020), Mpox (formerly monkeypox) caused by mpox virus infection (May 2022), Ebola caused by Ebola virus infection (October 2022), and Marburg virus disease caused by Marburg virus infection (April 2023) [23]. Some virus images are presented in fig. 1.

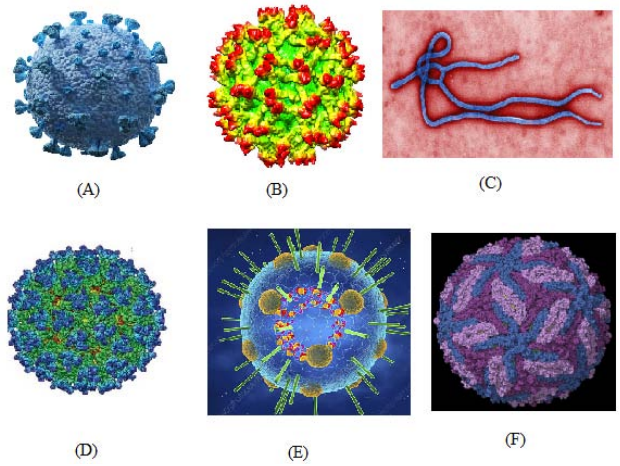

Fig. 1: (A) Corona virus, (B) Zika virus, (C) Ebola virus, (D) Alpha virus, (E) Myxo virus, (F) Flavi virus

Recent outbreaks and potential threats

Coronaviruses

The SARS crisis, caused by SARS-CoV, was one of the earliest occurrences of the twenty-first century. SARS-CoV first appeared in late 2002 and then quickly spread over the world before being contained by the middle of 2003. Several thousand instances were reported during this period, with a death rate of about 10% [24].

Yet another unusual zoonotic coronavirus, MERS-CoV, appeared in 2012 to cause MERS. Since 2012, there have been isolated outbreaks and cases of MERS. Even though the overall total of MERS-CoV cases is smaller, the fatality rate is significantly higher, nearing 35%. Finally, in 2019, SARS-CoV-2 emerged, triggering the present COVID-19 epidemic. All of these coronavirus virus strains have been linked to bats, with some passing through intermediary hosts such as camels and civet cats. Furthermore, several pre-epidemic groups I and II coronaviruses are circulating in bats that can replicate in basic human cells and are ready to emerge [25]. A global scenario of COVID-19 infections is represented in fig. 2.

Flavi viruses

The National Institutes of Health categorizes mosquito-borne flaviviruses as category A/B pathogens, such as dengue virus (DENV), Zika virus (ZIKV), West Nile virus, and yellow fever virus (YFV). DENV is prevalent in Southeast Asia and the Americas, with the development of novel strains every few years causing large epidemics since the early 2000s [26]. The Dengvaxia vaccination is approved in some countries for people who have previously had a DENV infection, but it is not recommended for people who have never had a DENV infection. ZIKV arrived from Polynesia in 2015 and quickly spread over South and Central America and the Caribbean. Although mortality rates were modest, newborn infants from infected mothers were born with catastrophic cases of microcephaly and other central nervous system abnormalities [27].

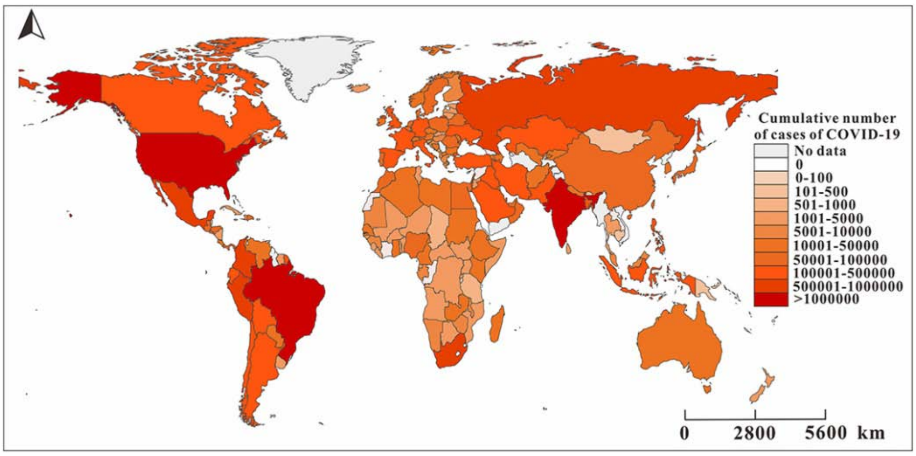

Fig. 2: Global scenario of COVID-19 infections

Influenza viruses

Throughout the 20th century, there were numerous outbreaks caused by influenza viruses. Among the most notorious was the deadly 1918 H1N1 flu pandemic, which claimed the lives of more than 50 million people worldwide. Additionally, there were several epidemics of highly pathogenic avian flu strains, including the H2N2 Asian flu in 1957 and the H3N2 Hong Kong flu in 1968. These strains also occasionally infect humans. In the 21st century, a new strain of influenza, the 2009 H1N1 swine flu pandemic, emerged, resulting in an estimated 250,000 deaths globally [28]. This strain, which was related to 1918 H1N1, was a triple reassortment of avian, swine, and human influenza strains. The twenty-first century has seen intermittent epidemics of avian H5N1, H7N9, and other influenza viruses with very high fatality rates in human cases but, thankfully, low human-to-human transmissibility. Major research efforts are underway to create universal influenza vaccinations and medicines [29].

Filo viruses

According to the NIH and the Centers for Disease Control and Prevention, the Filo viruses are classified as Ebola virus (EBOV) and Marburg virus (MARV) and are category A diseases. In the last decade, there were two major EBOV outbreaks. The pandemic between 2013 and 2016 mainly affected West African countries, with 30,000 people infected and a death toll of 40%. From 2018 to 2020, the Democratic Republic of the Congo experienced a second significant outbreak, with around 3,500 cases and a fatality rate of 65% [30].

The World Health Organization approved a highly effective vaccine candidate in 2019, and more than 200,000 individuals were immunized, helping to control the outbreak, while vaccination efforts were impeded by armed strife in the region. EBOV's major reservoir is bats, and the virus can spread directly to humans or through intermediate zoonotic hosts. EBOV can spread in the human population by contact with blood and body fluids, as well as through sexual transmission [31].

Alpha viruses

Chikungunya virus (CHIKV), an alphavirus, is naturally present in Africa and Asia. In 2006, India saw a significant outbreak, with over 1 million suspected cases. The virus subsequently spread to the Americas, generating huge outbreaks with several million infections between 2013 and 2016. CHIKV, like the flaviviruses listed above, is a mosquito-borne virus with a limited distribution, though this is expected to change due to vector proliferation and global climate change. Although seldom lethal, CHIKV infection can result in long-term debilitating chronic illness [32]. There is also a pool of other alphavirus family members (Venezuelan equine encephalitis virus (VEEV), Eastern equine encephalitis virus, Mayaro virus, and so on) that pose a real and growing threat to the health of communities and domesticated animals and are classified as category B pathogens by the NIH and CDC [34].

Other viruses of concern

There are several viruses within the Bunyavirales order that have caused epidemics or have the potential to create outbreaks, including Rift Valley fever virus (RVFV), Lass fever virus (LASV), Crimean-Congo hemorrhagic fever virus (CCHFV), and hantaviruses. There have also been small outbreaks of henipaviruses, such as the Nipah virus (NiV) outbreak in India in 2018, which had high fatality rates of 60-90% [34]. Bats are known to be a reservoir for henipaviruses, and intermediate hosts can include pigs and horses. To reduce transmission to humans, an equine vaccination has been developed for the Hendra virus (HeV). Norovirus is the major cause of gastrointestinal infections, causing repeated epidemics in the previous two decades that have resulted in severe sickness in children, the elderly, and immune-compromised adults, as well as 70,000-200,000 deaths worldwide. Because noroviruses are so varied, developing vaccines and antivirals may be difficult [35].

Recent advancements in treating viral infections

Antiviral medications can alleviate symptoms and minimize the duration of illness from viral illnesses such as the flu and Ebola. Antivirals are unable to eliminate the virus, which remains in your body. However, antiviral medications can render the virus dormant (inactive), resulting in little, if any, symptoms. Symptoms that appear while taking antivirals may be milder or disappear sooner.

Viruses have a rapid rate of multiplication as well as a rapid pace of mutation. The reason for this genetic mutation is viral resistance, which results in either a change in certain enzymes or a structural component of the virion. The rapid replication of the virus within the host cell results in the formation of a bigger gene pool from which mutations can emerge. Under these conditions, the selection pressure caused by antiviral medications results in the multiplication and spread of resistant viruses, resulting in the replacement of the susceptible population with the resistant one. Immunocompromised patients are the most vulnerable. According to the findings, AIDS patients suffer from serious diseases caused by resistant herpes viruses [36].

The next critical issue to address is anti-viral medicine cross-resistance. Resistance to one medicine is associated with decreased sensitivity to another drug of the same class. However, cross-reactivity between medication classes has been recorded. Acyclovir treatment of acyclovir-resistant herpes virus in AIDS patients results in herpes lesion healing failure. This is not the situation in immunocompromised patients. Thus, in some circumstances, viral resistance is clinically significant. However, this is still being researched [37].

The detection of viral resistance is critical. New methods for measuring viral resistance are being developed, with the most important being Polymerase Chain Reaction (PCR) for the identification of resistant genes, the use of cell lines that allow the use of a broader spectrum of viruses, and some improved methods of nucleic acid hybridization [38].

Several approaches have been proposed to reduce resistance, including the use of innovative treatment procedures wherever possible, avoiding continuous use of antiviral medications, and stopping usage of the drug wherever practicable.

Computational methods

It is now possible to uncover new lead compounds as medication candidates and multiple therapeutic agents for various parasite diseases by combining bioinformatics and computational approaches with publically available phenotypic data of host responses to pharmaceuticals and pathogens [39]. Computational technologies have found applications in both noninfectious and infectious disorders. However, parasite diseases receive far fewer studies. The two proteases of coronavirus, namely papain-like protease (PLpro) and 3C-like protease (3CLpro), have gained attention as targets for antiviral drugs due to their involvement in virus replication. [40].

***In silico* drug design**

According to reports, most antivirals approved before 2006 were based on natural ingredients. Although computational methods have been beneficial in guiding and expediting drug development, they are still too immature to deal with today's viral dangers promptly. Several viral diseases have been widely investigated computationally, but no breakthrough in the search for antivirals, as in the case of HCV, has occurred. *In silico* docking, investigations revealed 18 flavonoids with the ability to significantly bind with influenza haemagglutinin stems of diverse subtypes, which are antibodies' targets [41]. Target-based virtual ligand screening was carried out with 21 targets against compound libraries that included the ZINC drug database, natural products, and 78 regularly used antiviral medicines. This research suggested possible inhibitors for various targets. SARS-CoV-2 protease complexed with an inhibitor was utilized to screen approved medicines and clinical trial medications [41]. Candidate medications identified through docking studies include carfilzomib, eravacycline, valrubicin, lopinavir, and elbasvir. Carfilzomib was a promising SARS-CoV-2 inhibitor. Bioactive components from the medicinal plant were discovered to be potent SARS-CoV-2 inhibitors, including kaempferol, quercetin, demethoxycurcumin, apigenin-7-glucoside, naringenin, oleuropein curcumin, catechin, and epicatechin-gallate. Docking experiments also revealed that Nigellidine and-Hederin may be potential inhibitors of the SARS-CoV-2 virus, implying that the medical use of sativa against coronavirus infection warrants more investigation and attention [42].

Selenium-containing antiviral agents

Around 40 y ago, organoselenium compounds were discovered to have antiviral activity. Selenazofurin was reported as a ribavirin analogue with a broad spectrum for DNA and RNA viruses, being either virucidal or virustatic, depending on the virus type. In addition to inhibiting members of the Herpesviridae family, selenazofurin reduced influenza a virus (IVA) multiplication *in vitro* better than ribavirin; however, the results could not be verified *in vivo*. However, it appears to have promised anti-West Nile virus activity [43]. Selenazofurin was simply the beginning point for the development of a slew of other Se-containing antiviral drugs.

Anti-HIV medications even though the focus of researchers and the general public has switched to other viruses in recent years, HIV remains a significant health burden worldwide. In 1991, the first indication that Se-containing drugs could influence HIV was discovered [41]. Selenodiazole was the first Se-based non-NRTI to be published in the literature in 2009. However, it only suppressed HIV-1 replication and not HIV-2 [42]. Recently, novel organoselenium HIV antivirals targeting nucleocapsid protein 7 (NCp7), which plays an important role in HIV replication, were described. Interestingly, NCp7 is largely conserved among HIV strains, and resistance strains are not favored when it is inhibited. Compound 15 is a strong and selective anti-HIV-1 and anti-HIV-2 drug with a low toxicity profile, even against resistant HIV-1 strains (EC50 3.31 and 3.18 mmol, respectively). Proteomic research demonstrated that DISeBA-treated latently infected cells accumulate unprocessed Gag poly-protein, a precursor to NCp7, implying that compound 15 recognized NCp7 early [42]. Synthetically difficult 1,2,3-thiaselenazoles, such as compound 16, have recently been postulated as possible HIV agents. This tiny series was examined in a feline immunodeficiency virus (FIV) model, which shares several similarities with HIV, including a nucleocapsid protein. A more recent study revealed another potential target of ebselen; the molecule was discovered to disrupt HIV's interaction with lens epithelium-derived growth factor (LEDGF, also known as p75), an essential cellular cofactor that HIV hijacks to integrate into the host cell. More research is needed to determine the precise mechanisms of ebselen's HIV-inhibition abilities [44].

Molecular docking

Docking approaches evaluate the fitness of a connection between small molecules of substance and viral proteins using a known 3D structure in the setting of drug repurposing for the invention of therapies against viral infections. Fitness (or binding affinity) is generally calculated as potential energy resulting from force fields operating on interacting molecular particles. Lower potential energy values (greater binding affinity) correspond to more stable structures for complexes combining the small molecule and the viral protein and are more likely to be involved with ligand-mediated neutralization of viral protein activity [45]. As a result, tiny compounds with a high affinity for viral proteins are prioritized as potentially repurposable medicines. GLIDE, AutoDock Vina, and SwissDock are some of the well-known docking technologies and software packages. The algorithms, scoring systems, docking type (flexible or rigid), and docking elements (for example, protein-protein, protein-ligand, protein-peptide) used by the packages differ. Parks and Smith have discussed the potential benefits of molecular docking for rapid medication repurposing against SARS-CoV-2 [46].

The lack of a solved structure for SARS-CoV-2 viral proteins posed a hurdle in the early research. One solution is to rely on sequence conservation and assume 3D structure conservation between SARS-CoV-2 and other coronaviruses, particularly SARS-CoV-1.

Molecular imaging

Pathogen-specific imaging for viral infections would rely on either the production of recombinant viruses encoding reporter molecules, as has been done for BLI, or the generation of radiolabeled probes that are selectively retained at sites of infection [39]. If techniques for imaging viral infections in large animals or humans can be developed, the ultimate goal will be to visualize host responses and viral replication at the same time to determine the relationship between pathogen spread and processes such as the release of proinflammatory mediators, the influx of inflammatory cells, apoptosis of infected or bystander cells, and changes in vascular function [40].

Viral proteins

Other viruses' capsid-binding compounds have been examined. Capsid-binding inhibitors are being used to combat HBV. While the chemicals boost the rate of capsid development at substoichiometric concentrations, at high concentrations, they misdirect capsid formation and induce the production of abnormal structures. The mechanism by which the compounds inhibit viral replication is still unknown; it is possible that the compounds do not directly inhibit HBV replication, but rather disrupt the coordination of capsid assembly with other stages of replication, or inhibit structural transitions required for the formation of mature, infectious capsids [47].

Ribonuclease targeting chimera (Ribotac)

RIBOTAC is a novel RNA degradation method. RIBOTAC consists of an RNA-binding small molecule and an L-recruiting ribonuclease (RNase) module designed to break down the viral genome [48]. RNase L is involved in innate immunity and is expressed at low levels in all cells as an inactive monomer that is activated and dimerized upon viral infection with inherent substrate specificity [49].

Proteolysis targeting chimera (Protac)

PROTACs have emerged as a novel drug discovery paradigm for targeting proteins by encouraging and realizing target protein breakdown via the ubiquitin-proteasome system (UPS) [50]. PROTACs are hetero-bifunctional molecules that include a protein of interest (POI) ligand, an E3 ubiquitin ligase recruitment ligand, and a linker. To decrease the distance between them *in vivo*, bifunctional PROTAC molecules attach to the POI with one end and an E3 ligase with the other. The E3 ligase subsequently mediates the transfer of ubiquitin from an E2 enzyme to the POI, which is then degraded by the proteasome [51]. This methodology has recently been steadily used in the discovery of antiviral medicines.

Topology-matching design

Influenza A virus (IAV) is an enclosed RNA virus in which the membrane attaches two viral proteins that govern virion-host cell interactions, namely (HA) and neuraminidase (NA). The IAV virion, from a topological standpoint, is a nanosized particle of roughly 100 nm with a spiky surface generated by the HA NA. To accomplish competitive binding with the virus/cell interface, nano-inhibitors must match the virion's size and structure [52].

The nano-inhibitor might neutralize the viral particle extracellularly, preventing it from attaching to and entering host cells. The viral replication was significantly reduced by six orders of magnitude, with more than 99.999% inhibition even after infection, demonstrating that such a nano-inhibitor could be a powerful anti-influenza agent. They also discovered a spiky nano-inhibitor with topography similar to IAV virions. The binding of the nanostructures with spikes between 5 and 10 nm was significantly higher than that of smooth nanoparticles due to the short spikes inserted into the glycoprotein gap of the IAV virion. Furthermore, using an erythrocyte membrane (EM) to target IAV could effectively prevent IAV virion binding to the cells and suppress further infection. EM-coated nanostructures inhibited viral proliferation by more than 99.9% in a post-infection assay [50].

The same group published hetero-multivalent topology-matched nanostructures as potent and broad-spectrum IAV inhibitors in 2021. The hetero-multivalent binding was translated to bowl-like nanostructures with spherical surfaces.

Role of nanotechnology in treating viral infections

A nanopharmaceutical is any nanomaterial that has medicinal potential, such as dendrimers, liposomes, micelles, or nanocapsules. These can act as therapeutic agents by dissolving, entrapping, encapsulating, adsorbing, or chemically attaching the medication. Nanoparticles come in a variety of shapes and chemical compositions, and they can be classed based on how medications are administered or the features of the matrix from which they are made. Based on their composition, we describe the most popular forms of nanocarriers (fig. 3) utilized for drug delivery.

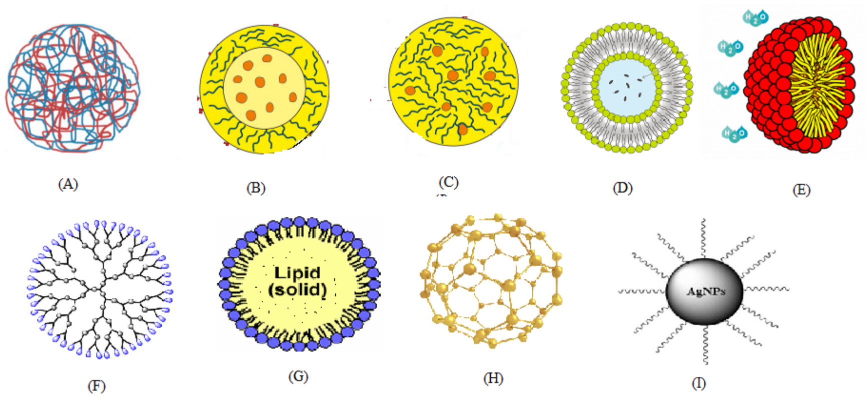

Fig. 3: Nanoparticles for treatment of viral infections. (A) Polymeric nanoparticles, (B) Nanocapsules, (C) Nanospheres, (D) Liposomes, (E) Micelle, (F) Dendrimers, (G) Solid lipid nanoparticles, (H) Gold nanoparticles, (I) Silver nanoparticles

Organic nanoparticles

Organic nanoparticles are the most thoroughly explored type of nanoparticle for drug delivery and the most widely authorized therapeutic system in humans. The following are the most frequent forms of organic nanoparticles.

Polymeric nanoparticles

Polymeric nanoparticles are colloidal solids measuring 10 to 1000 nm in size. The tiny size can aid capillary penetration and cell uptake, leading to higher concentrations in target areas. Polymers approved for use in medicine and pharmaceuticals by the World Health Organisation (WHO) and the Food and Drug Administration (FDA) include polylactides (PLA), polyglycolides (PGA), and poly(lactide-co-glycolides) (PLGA). Because of their higher biocompatibility and biodegradability characteristics, poly(D, L-lactide-co-glycolide) (PLG) and PLGA-based nanoparticles are the most commonly employed [53]. Surface modifications with hydrophilic polymers such as PEG are essential for reducing non-specific interactions with serum proteins, decreasing susceptibility to opsonization, and deferring uptake by phagocytosis, thereby expanding the drug half-life and further affecting the biodistribution and pharmacokinetic profile of the drug, and are thus considered the 'gold-standard' of cloaking agent systems. Polymeric nanoparticles can be divided into two types: nanocapsules and nanospheres [54].

Nanocapsules

Nanocapsules are hollow spheres with a polymer coating that contain the medicine in an inner cavity. They have a size range of 50 to 300 nm and are distinguished by their low density and high loading capabilities [55].

One example of the usage of nanocapsules in increasing drug distribution is the permeability glycoprotein (P-gp) efflux transporter, which may impede antiviral delivery to brain tissue. SolutolR HS15 is an excipient that inhibits P-gp, enhancing medication distribution across the BBB. This study found that SolutolR HS15 nanocapsules loaded with the HIV protease inhibitor indinavir dramatically boosted absorption in the brain and testes of mice as compared to control mice given only indinavir solution [56].

Nanospheres

These are matrix systems in which the drug is physically or evenly disseminated and has diameters that vary from 100 to 200 nm. Several research investigations have been conducted employing nanospheres in the management of hepatitis B virus (HBV), herpes simplex virus (HSV), and influenza, as well as thorough review publications on the use of these agents in viral treatment [57].

Liposomes

Liposomes are spherical carriers that range in size from 20 to 30 nm. They are made up of a phospholipid bilayer with an aqueous core (which can resemble cell membranes and directly merge with microbial membranes). Hydrophilic and lipophilic medicines (or other biologically active chemicals) can be incorporated into the phospholipid bilayer or the inner aqueous cavity, respectively. Liposomes also have the advantage of being largely non-toxic and biodegradable. Because of their propensity to act as immunological adjuvants, liposomal formulations have been extensively explored in vaccine research [58].

Micelles

Micelles have sizes ranging from 10 to 100 nm. These are made up of an inner hydrophobic core (which can include medications that are poorly water soluble) and an exterior hydrophilic polymer (such as PEG, which can extend circulation time and improve accumulation). Polymeric micelles, for example, have received a lot of interest as drug delivery agents with substantial therapeutic promise [54]. One of the most appealing nanotechnologies for improving the water solubility and stability of otherwise technologically constrained (poorly water soluble and unstable) pharmaceuticals is drug encapsulation with polymeric micelles. Another advantage of utilizing micelles in therapy is that they dissociate at a slower rate, allowing for longer drug retention time and, finally, increased drug accumulation at the target site [55].

Dendrimers

Dendrimers are symmetrical, macromolecular, hyper-branched structures that radiate from a central core via connectors and branching units, with terminal groups controlling interaction with its target environment. These are globular in shape and are divided into three separate domains (central core, branches, and terminal functional groups). They have increased usefulness due to their capacity to encapsulate various chemical moieties and inner layers and exhibit multiple surface groups (multivalent surface) [59].

Solid lipid nanoparticles

Solid lipid nanoparticles (SLNs) are an alternate drug delivery technique to the previously described colloidal nanoparticles. The use of SLNs tries to combine the benefits of traditional nanocarriers while avoiding some of their drawbacks. Large-scale manufacturing of polymeric nanoparticles, for example, is a significant problem, limiting their value in drug delivery, whereas the manufacture of SLNs can be accomplished in both cost-effective and relatively straightforward ways (e. g., using high-pressure homogenization and microemulsion techniques). When compared to synthetic polymer nanoparticles, SLNs have higher stability, safety, and availability, as well as lower toxicity and superior drug-release characteristics [57].

Inorganic nanoparticles

Metallic nanoparticles can be much smaller than organic nanoparticles, ranging in size from 1 nm to 100 nm, yet their loading efficacy is significantly higher. The synthesis of metallic nanoparticles can be divided into two approaches: the 'bottom-up' (or self-assembly) approach refers to building the nanoparticle level by level (e. g., atom by atom or cluster by cluster), and the 'top-down' approach uses chemical or physical methods to reduce the inorganic material to its nanosized form. The reaction parameters (pH, temperature, duration, or concentration) can be employed to adjust nanoparticle attributes (size and shape), whilst the reducing agent used can influence aspects such as loading capacity, release, and aggregation profiles [54, 60].

Gold nanoparticles

Gold nanoparticles (GNPs) are frequently studied as nanocarriers due to their outstanding conductivity, surface modification flexibility, biocompatibility, and simple manufacturing procedures. The gold core (which is inert and non-toxic), photophysical capabilities (which can promote efficient drug release at faraway places), and variety of functionalization via thiol linkages are all advantages provided by their unique physical and chemical qualities.

Silver nanoparticles

Silver nanoparticles are the most effective metallic nanoparticles against bacteria, viruses, and other eukaryotic microorganisms, owing to silver's inherent inhibitory and bactericidal potential and their good conductivity, catalytic properties, and chemical stability. Silver nanoparticles' main modes of action are the release of silver ions (which increases antibacterial activity), cell membrane rupture, and DNA damage. The reader is directed to a comprehensive overview of the use of silver nanoparticles as virucidal agents.

Other metallic nanoparticles

Other metallic nanoparticles with antiviral properties include titanium, zinc, and copper, as well as metal oxide nanoparticles like iron oxide, zinc oxide, and titanium dioxide. Others, such as platinum nanoparticles employed to detect influenza virus, have yet to be studied [60, 61].

CONCLUSION

New technologies are expediting the process of developing virologic treatments, with the inevitable shift towards newer and easier-to-use platforms. Simultaneously, the ongoing discovery of new viruses is drastically extending the world of medical virology and propelling the development of medicines capable of detecting an ever-increasing range of viral diseases. We are witnessing a technological revolution that has radically revolutionized the treatment of virus infections with methodological breakthroughs that will not displace their predecessors but will instead add to the expansion of the virology toolkit. From this vantage point, we are living in exciting times that will propel the discipline forward and have a tremendous impact on patient care.

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All the authors have contributed equally.

CONFLICTS OF INTERESTS

Declared none

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