EXPLORING BIO-NANOMOLECULES FOR ADVANCED STRATEGIES IN TREATING VIRAL INFECTIONS: A COMPREHENSIVE REVIEW

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Abstract

Globally infectious diseases are the leading risk factor for death, with viruses having a particularly large influence on healthcare and socio-economic development. Additionally, the fast development of medication resistance to presently available medicines, as well as harmful side effects from long-term usage is a major public health concern. Nanomedicine technology is developing as a novel technique capable of overcoming the limitations of molecular treatments and increasing their anti-infective activity by site-specific delivery to infection sites, lowering off-target effects and/or control of resistance emergence. NPs have distinctive physical features that are important in administration of drugs. Nanotechnologies have therapeutic applications and the potential to aid in the detection of viruses and viral diseases in the laboratory. Virus-like particles (VLPs) have minimal side effects and are safe and non-toxic, it has an interior hollow area; they are often used as nano-drug carriers. Up to date biopharmaceutical engineering is becoming a prominent topic.

Keywords: Immunomodulatory drug, Nanomevaccine, Viral infection, Hepatitis virus, Nanovaccine.

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1. Introduction

Viruses are not usually damaging species since they have various valuable applications in bio-medical, bionanotechnological & microbiological antimicrobial agents, applications of vaccine synthesis and food material creation. Although their useful properties, the phrase viruses can refer to frequently lead to death in the general population, in additional of some exceptionally emphasis Corona virus, Dengue fever, A H7N9 virus, SARS, HPV, Ebola and AIDS are all devastating infections that cause significant death and morbidity rates. It's possible that there are more negative consequences than favorable consequences [1, 2].

In the last three decades, medical diagnostics has seen major technical improvements in the detection of viral illnesses. The Enzyme - linked immunosorbent assay technique was widely used in labs to identify viral infections throughout the 1980s. The tests may identify antibodies or IgG, IgM, and IgA to viral or infectious antigens due to their unique design. The fast development of the (PCR) and its variations, along with their use in viral and infectious illness detection, in the mid-1980s and beginning of this decade. We are now observing the emergence of a new area in the latter half of the century, including researchers nearly the edge to develop the uses in the area of nanotechnology (NT) medication. Word "nanometer" refers to a tenth of a measure metre (10^{-9}). The field of NT includes atomic and sub atomic level technologies concerned working with tools smaller than 100nm in size, as well as their creative applications. The finding and creation of carbon materials, a class of unique empty carbon molecules assemblies, sparked research in this topic in the 1980s. Such biomolecules were biodegradable and had no genotoxic or mutagenic properties. Nanomolecules have applications in medicines, medical applications, infectious illness diagnosis and therapy [3].

Viral Infection (HBV) is a DNA virus that causes roughly 400 million people worldwide individuals globally on a chronic basis. Cirrhosis and hepatocellular cancer have been linked to HBV replication [4, 5]. Viruses central particle find their way towards the nucleus. When HBV virions reach the hepatocyte, when its genetic material is fixed to give a covalently closed circular DNA (cccDNA) templates for infectious (mRNA) and 3.5 kb pre-genomic RNA (pgRNA) generation [6],[7]. The pgRNA serves as a model for reverse transcriptase and the production of genomic sequences [8]. Hence, pgRNA transcription from cccDNA is an important process in HBV imitation Six medications for such treatment of severe Hepatitis b were approved before 2007. Two of them are immunomodulatory medications, standard interferon (IFN)-2b and pegylated interferon (IFN)-2a, which attempt to reestablish host immunological control over HBV, resulting in long-term disease recovery. The other four treatments are nucleoside analogues with direct antiviral action (lamivudine, adefovir, entecavir, and telbuvidine) [9]. IFN-also causes both T-lymphocytes, CD^{8+} cytotoxic and NK cells to lyse infected hepatocytes [10], and it can also directly reduce viral protein production by influencing the activity of antiviral cytokines [11]. The use of IFN-, on the other hand, is limited by substantial adverse effects and low effectiveness rates [12]. Nucleoside (t)-ide variants primarily block the viral polymerase reverse transcriptase. Although nucleoside analogue therapy for chronic HBV Infection (CHB) inhibits Viral replication in the short term, due to the advent of HBV strains that are resistant to drugs, this effect is not always prolonged figure 1[13].

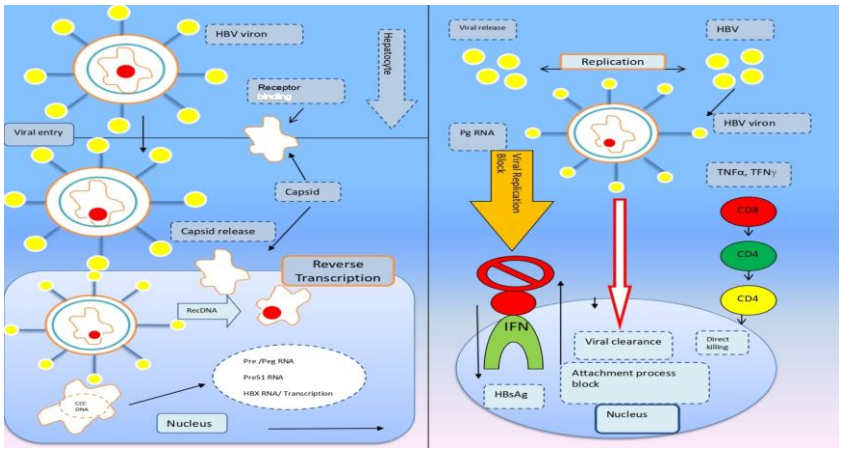

Figure 1: HBV virus mechanism in CD8 & CD4 cells with the help of nanoparticles for the clearance of virus.

As a result, it is necessary to formulate novel antiviral methods to address both HBV infections, including adventurous and variant. While metal NPs have been widely studied in catalysis and optoelectronic devices [14, 16], there's been comparatively little research on their biological characteristics and possible therapeutic uses [17, 18]. The antimicrobial properties of silver NPs (AgNPs) have attracted the greatest interest in this respect, with proteomic & biochemical investigations into the antibacterial or antifungal activities of silver NPs published [19, 20]. At present there are just few published studies on the anti-viral activities of AgNPs in the literature, both of which reveal anti-HIV-1 capabilities. It was discovered that AgNPs may cling to HIV virus particles in a predictable pattern and block the virus's ability to bind to host cells. Moreover, AgNPs can suppress HIV replication and have promised powerful antioxidant properties against HIV-infected T-cells [21, 22].

In this review we discussed about the relevant literature of most recent (past 10 years), which describe the nanomedicines (NM) technology and useful in the laboratory diagnosis of viruses and viral infection. Applications mechanism and treatment were also studied in this review in a detailed manner.

2 Inorganic NPs and their significance

Metallic NPs can be significantly lesser than organic NPs, range in size from 1nm to 10nm, yet their loading effectiveness is substantially higher [63]. The synthesis of metallic NPs can be divided into two approaches: the "bottomup" or the "topdown" technique involves physio-chemical processes to decrease the amount of inorganic material towards, nanometric form, whereas the "self assembly" method explains the development of the step by step, NP (e.g., atom by atom or cluster by cluster). [64]. Various reaction parameters pH, heat, duration, or dosage) may be utilised to vary the NP properties shape and size, while the reductant employed can have an impact on variables like load bearing capacity, discharge, and aggregating profiles [65].

2.1 Gold (AuNPs)

AuNPs are frequently studied as nano-carriers owing to their unique conductivity, surface modification flexibility, biocompatibility and simple manufacturing procedures. The gold nucleus which is immobile and non-hazardous, photochemical capabilities, which can promote effective drug release in remote places & diversity of functionalization via redox linkage are some of the additional benefits provided by their distinctive physochemical qualities. There are fundamental AuNPs preparation techniques that can yield NPs with varied diameters 1–2nm, 1.5–5nm or 10–150nm, depend on the application) figure2 (a) [66].

2.2 Silver NPs (AgNPs)

AgNPs are the mainly efficient metallic NPs next to viruses, bacteria, and other eukaryotic organisms, owing to silver's intrinsic antimicrobial and suppressive capabilities, other than they have high electrical resistance, characteristics and physo-chemical stability. The production of Ag ions, which boosts antibacterial action, cell covering rupture and DNA break, are the primary modes of action of silver AgNPs. The reader is directed to a comprehensive overview of the use of AgNPs as virucidal agents figure2 (b) [67].

2.3 Organic NPs commonly used therapeutic system in humans

Organic NPs are the most thoroughly explored form of NP for medication administration and the most commonly used therapeutic system in humans [68]. Following are the most prevalent forms of organic NPs (Figure 2).

2.3.1 Nanocapsules

Nanocapsules are spherical cylinders with an interior chamber enclosed by a polymer covering that contains the drug [69]. They have a size range of 50 to 300nm and are distinguished by their light weight and soaring payload capacity [70, 71]. Anti-viral delivery to cerebral cortex may be limited due to the permeability of the glycoprotein (P-gp) efflux carrier, which is used as examples of how nanocapsules might be used to increase medication delivery. Solutol® HS15 is an excipient that inhibits P-gp, enhancing medication distribution across the BBB [72].

According to the outcome of this investigation, Solutol® HS15 nanocapsules preloaded with the HIV combination therapy that exhibited considerably higher absorption of testes & brain of mice as in comparison to control animals given just indinavir [71].

2.3.2 Nanospheres

These were mechanical components in which the drug is physically or evenly spread and has a range of 100 to 200nm. Several research have been conducted on the usage of the nanospheres in the therapy of (HBV), (HSV) and influenza have been undertaken, and extensive review papers the

use of these drugs in viral therapy are also available [67].

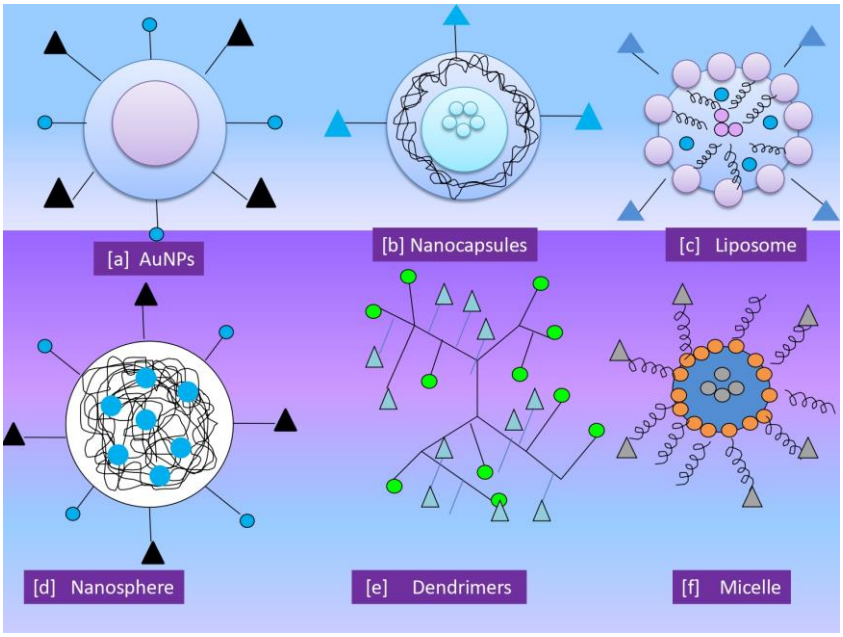

Figure 2: Common examples of nanocarriers used for anti-viral drug delivery, (a) AuNPs, (b) Nanocapsules, (c) Liposome, (d) Nanosphere, (e) Dendrimers, (f) Micelle

2.4 Advantages of Nanomolecule in virus treatment

Nanotechnology has enabled incredibly sensitive detection devices capable of identifying molecules in the nano molar range. Although these developments were not originally intended for the identification of viral components, their use in virus detection has increased dramatically in the last decade. The analysis of avian influenza virus proteins at femto molar levels using amperometric sensors is an example of a cutting-edge, cutting-edge detection system made possible by nanotechnological instruments. In these detection systems, metal and metal oxide NPs play a crucial function by supplying a steady, reactive, and appropriate adhesive sites for ligand identification [113].

NPs have been exploited as antiviral agents as well as biocompatible medication carriers in the last decade. The use of nanotechnology as antiviral, lower the danger of drug conflict, and it is more common with molecular antiviral. More than any other NP, AgNPs include antiviral treatment. However, by the introduction of ZnNPs, which show fresh, assure as efficient adjuvant and antigen-presenting platform [114], this tendency is shifting.

These NPs capture the herpes viral particles, preventive to transmit a disease, as a result, eliciting an immune-genic reaction through antigen-presenting cell. The innovative therapeutic paradigm, known as microbivac, has the potential to open the path for long-term treatment of chronic viral illness utilising nanomaterials. Finally, there is hope for such production of inhibition, biodegradable metal-based NPs HSV antiviral drugs that might be used in the clinic soon. [115].

3.0 Application of Nanotechnology in Viral Detection and treatment

3.1 Hepatitis B virus (HBV), Hepatitis C virus (HCV) and Hepatitis E virus (HEV)

A method for detect genes via visually labeled gene probes tagged with AuNPs has been presented. The screening probe was a 5-end-amino-derivatized oligonucleotide fixed on a glass surface and the collecting probe was an NP supported oligonucleotide with 3-end-mercapto-derivatization. To visually identify the target DNA, sandwich hybridization with highly sensitive nanoamplification and Ag staining were utilized. Chips carrying HBV/HCV genes Au/Ag NP stain extension have been discovered to be successful in recognizing these viruses were discovered in patient samples. The resonant Rayleigh light scattering (RLS) spectroscopy was employed as a diagnostic readout to monitor gene probe immobilization on AuNP surfaces [23].

A protein chip technology with nanogold immunological amplification and Ag staining was applied to discover antibodies to HBV & HCV components at the same time. As substantial bases, glass slides are employed (protein chips)

for immobilising HBV and HCV antigens HBeAg, HBsAg, and HBcAg a combination NS3, NS5, and core antigens are all present. The test is used for colloidal nanogold labeled staphylococcal protein A (SPA) as an indication. The immune-gold Ag staining advance method was utilized to improve the exposure signal. As consequence, a dark black pattern was visible with the naked eye at an array location. The technique could identify specific antibodies at levels as low as 3mg/mL [24]. The use of nanogold-labeled oligonucleotide probes in combination with Ag stain amplification and the micro-array approach resulted in the development of an arraybased nanoamplification technology for the exposure of HEV. As the capturing probe, the 5end-NH_2 mutated oligo-nucleotide probes are immobilised on the DNA chip base. The diagnostic probe is made up of a 3-end-SH oligo-nucleotide probe and a nanogold colloid. The HEV viral RNA was amplified using such a one-step RT-PCR amplification technique and the cDNA on a microarray, was hybridised with the capturing and identification probes. The information was enhanced via Ag stain amplification, which could be seen with the naked eye. Microarrays were able to identify 100fM of amplicon for as little as 2 minutes of picture development time. A similar method is given for HAV [25, 26].

3.1.1 Treatment

However, there are many peer-reviewed studies on how NPs have been/are being used to distribute chemotherapeutic drugs to viral sites. Very few papers have shown the true delivery system intended, diagnosis of hepatitis in person to person or animal concepts [82], who revealed the therapies of hepatitis virus via HA-AuNP/IFN advanced Hyaluronic acid AuNP/ IFNλ. The medication was compare to a traditional polyethylene glycol and tagged with IFN method and it was reported that the new NPs had similar natural activity while being more stable in human serum. Further studies found that using gold nanorods in hepatitis patients might accelerate the damage of liver and enhance hepatitis rigorousness [83]. The investigation also said such findings are only supported by gene expression and flow cytometry, assays and that even at low concentrations, Au-nanorods produce significant polarisation of liver macrophages. Recent study found that when AuNPs are incubated for a particular amount of time, they have no interaction with the hepatitis C virus [84]. This 30 sample study revealed no difference in variation in the action of basic viral load and AuNP treated viral load, suggesting, AuNPs cannot be employed straight as antiinfective agent for the HCV. SPIONs linked to DNA enzymes have already been utilized to kill the hepatitis C virus in a similar way to that outlined above for the successful elimination of the hepatitis virus [85].
SPIONs are used not just to act as magnetic anchors for desirable molecules also as fluorescent probes in MRI. SPIONs coated with lipid and coated through antiviral drugs with vaccinations can also transport their carrier loads to specific sites [86]. In some other previous work, Ag and Au nano-clusters coated by polyvinylpyrrolidone [87], were able to transport greater payloads such as DNA enzyme to the target location when compare to vacant nano-shells created for drug discharge objectives. The low amount of findings suggests that study on use of NPs in treatment aspect of virology are silent in their early stages and might be a promising field for future work.

3.2 Human Immunodeficiency Virus

This unique NP-based Biobar Code Amplification assay for such quick and sensitive detection of HIV-1 envelope p24 antigens had previously been developed. The anti-p24 antibodycoated-microplates collect viral antigen p24, which is then connected to a detecting mono clonal antibody labelled with avidin as the diagnostic probe. For signal enhancement, streptavidin-coated NP-based biobarcode DNAs detect this immunological complex. A chip-based scanometric approach is used for signal detection. The customised BCA test was 150 times more accurate than standard ELISA, detecting as low as 0.1pg/mL. Furthermore, in seropositive tests, the BCA test detect HIV-1 infection in three days quicker than ELISA, indicating that it could be employed as an alternate diagnostic tool for HIV RNA identification [27].

3.2.1 Treatment

Gold and AgNPs have also dominated HIV and prophylactic/therapeutic models, followed closely by super paramagnetic iron oxide NPs. The trans activator of transcription protein is used as an activator in a number of studies utilizing metal and metal oxide NPs to targeted cells of interest for intravascular transfer of NPs [73, 74]. As a result, the presence of viruses is unable to adhere to accommodate cells, blocking infection. AuNPs have a dynamic surface and rapidly bind to sulfated biological ligand. This, together by their superior conductivity, biocompatibility, and ease of manufacture, makes them a viable substance with antiviral properties. To develop preventative

glycoNP antiretrovirals, AuNPs were coupled with elongated (oligo) mannosides of the elevated undecasaccharide Man GlcNAc.

In this situation, a small quantity of AuNPs can provide substrate for sugar adhesion and assembly. Furthermore, AuNPs anti-gp120 action provides for a synergistic effect when combined with glycoconjugates. The scientists also mentioned that the use of another very effective antiviral glycol-conjugate tag with AuNPs [76] and N-linked high-mannose glycans, which opens new a venues for anti-HIV therapy. Using carbohydrate-coated AuNPs loaded with anti-HIV prodrug options pH-mediated release of abacavir and lamivudine paradigm, researchers later designed a highly active antiretroviral treatment (HAART). AuNPs provide excellent attachment sites for the adsorption of a variety of ligands. Although AgNPs have been shown to exhibit anti-HIV effects at non-cytotoxic doses [76], the technique under work was examined later.

According to the research, AgNPs show anti-HIV activity at such a preliminary phase of virus assembly, most commonly as a virulent compound or as an inhibition of viral entry by interacting with the viral protein glycoprotein120 and prevent CD4-dependent virion attachment, synthesis, and pathogenicity. Following this investigation, a spermicidal gel comprised with AgNPs and covered with polyvinyl-pyrrol-idone and it is prepared as a genital micro-bicide for the prevention of HIV transmission [78]. In vitro, AgNPs and Strong reducing antibodies have been discovered to provide an additional effect against HIV-1 infection in cells [76]. Further research on the inclusion of AgNPs into condoms [76] and the increased suppression of HIV protease by AgNPs [76] demonstrate the significance of Ag in HIV treatment.

Anti-retro-virals with high potency treatment for HIV has been shown to be, very effective strategy for eliminating dynamic HIV from the body by restricting HIV replication. Hidden HIV, on the other hand, increases the risk of illness relapse, impeding total elimination. As a result, innovative ways of treating superparamagnetic iron oxide NPs are used to create these forms (SPIONs). Mononuclear phagocyte ghost cells, including monocytes in the blood, macrophages in the tissues, microglial, and dendritic cells in bone marrow, are being employed as covert delivery vehicles for antiretroviral medicines to HIV latent forms. Magnetic resonance imaging (MRI) was used to examine the distribution of indinavir-loaded bone marrow macrophages and SPIONs throughout the body [79].

Drug levels were high, exceeding 200–350 times the therapeutic concentration from day1-14 according to the data. Magnetic-hyperthermia, employs SPIONs and an magnetic field that alternates to create heat above 45°C and has been employed in anti-HIV therapy. SPIONs were employed to target HIV's latent reservoirs and were thermo-ablated to boost HIV-infected cells' cytotoxic T-lymphocyte targeting cell [80]. Magnetically directed layer-by-layer nanocarriers were employed to co-encapsulate a lag agent and an anti-HIV drug (tenofovir) for the exposure of neuro-AIDS (vorinostat). SPIONs with a bilayer coating enhanced drug challenges to ensure (2.8 times for tenofovir) and drug delivery (30 times with 100% discharge) during five days [76].

SPIONs are used to pass across the blood-brain barrier (BBB) Once labeled on SPIONs then loaded using PMA amphiphilic polymers, the complex structures drug enfuvitride, which would be difficult to permeate the Blood brain barrier, was enabled to do it anyway. The study demonstrated that in order to entirely eliminate HIV, new studies that remove the BBB must be considered, and SPIONs play a key part in this. [81]

3.3 Influenza

Influenza is a highly contagious respiratory illness [52], with outbreaks linked to morbidity all over the world [53], with yearly epidemics and occasional pandemics resulting in millions of fatalities. Antigenic shifts and genomic changes across influenza species result in a significant degree of variety, allowing the creation of novel influenza strains as well as medication resistance. New strains continue to arise, posing a public health risk [55]. Sirnaomics' STP702 (FluquitTM) is a nanotherapeutic polymer-based is now in preclinical testing. This includes single stand RNA that targets influenza's conserved areas for antiviral efficacy next to avian flu, swine flu, and the newly discovered H7N9 pandemic influenza [56].

Thermoresponsive hydrogel particle known as "Nanotraps" are able of trap are live transmittable viruses, viral RNA and proteins [57]. This sort of innovative technology has the potential to be applied to the treatment of transferable illnesses such as the influenza virus. To deliver glycosyl

sialyl neolacto-N-tetraose c (LSTc), Liposomes were used in combination with sialoside, asynthesized deception receptors for influenza interaction. These liposomes were discovered to be extremely effective at capturing and trapping influenza 'A' viruses in a competitive manner, as well as inhibiting infection of target treated cells [58].

Hemagglutinin (HA) and neuraminidase (NA), two influenza glycoproteins, are important in virus assembly (to sialic-acid-containing cell surface receptors) and discharge, accordingly [59]. Oseltamivir is a NA blocker that stops influenza from spreading from cell to cell and keeps it going. In vitro, oseltamivir-modified AgNPs effectively reduced H1N1 illness by reducing both HA and NA activity. The antiviral effects of these nano-constructs were shown to be aided by the suppression of DNA breakage, condensed chromatin and caspase-3 activation. When compared to oseltamivir controls, the toxicity characteristics of these oseltamivir-modified AgNPs were also shown to be elevated in MDCK cells, as measured by cytopathic effect, TEM, and cell viability assays [61].

Another investigation found that a polylysine linker was used to produce (TiO2) NPs were successfully prepared targeting the 3′ non-coding region of the influenza virus using DNA pieces A virus. These nanocomposites were successful in achieving penetrate cells without the need for transfection agents and were shown to be effective influenza 'A' virus inhibitors in vitro. Irregular DNA sequences, unattached in the presence of DNA fragments of NPs and naked NPs all had minimal antiviral effects in the control samples [62].

3.3.1 Treatment

It asserts that the state of art of NP based therapy strategies for combating certain respiratory infections (PI-3V, influenza or RSV) has been thoroughly explored. The majority of substantial research in the field of therapeutic medicine relies on the use of polymeric NPs for this purpose. While polymeric NPs play an important role in therapeutic nanotechnology, metal and metal oxide NPs have been used in numerous studies, particularly for the suppression of the influenza virus. While AuNPs have not been found to directly suppress the influenza virus, their use in assessing the efficiency of particular vaccinations has been important [88].

A mouse flu paradigm as challenge was conducted; AuNPs bound to the influenza matrix protein 2's conserved extracellular region 'A' virus was used for testing the vaccine's potency [89]. On the other hand, surface-activated anionic AuNPs have demonstrated extraordinary antiviral efficacy against the influenza virus. While vaccinations are quite distinct from their viral equivalents, AuNPs surfaces that are actuated demonstrated by assuming active positions areas on the virus, the virus is rendered inactive [90]. When it concerns to inhibiting influenza viruses, AgNPs are unrivalled. Because of their efficacy in blocking influenza viruses, their application to other viruses has been foreshadowed. Over the years, the use of AgNPs for the suppression of influenza viruses has been widely researched [91].

In their initial investigation, they reports on AgNPs therapy with the H3N2 virus. According to the findings, AgNPs preferentially demolish the viral genome appearance in between 30min and 2 hours. In vitro tests demonstrated, while AgNPs had no direct toxic effect, they had a considerable impact on cell survival while treated with H3N2 virus [92]. AgNPs had a toxic concentration of 25g/mL, whereas the [TCID50] tissue culture infectious dose of the influenza virus H3N2 had a concentration of 10–3.5g/mL in MDCK cell lines.

In addition the endurance rate of Madin-Darby canine kidney cells was found to be 98 percent following a 50 g/mL AgNP forming a positive with 40 TCID50 of flu virus H3N2 over 2 hours, whereas the mortality percentage of MDCK cells in the flu virus H3N2 control condition with 20 TCID was 35 percent. AgNPs (25g/mL) substantially inhibited MDCK cell death produced by the 20 TCID50 influenza viruses H3N2. Later research by the same group revealed comparable effectiveness against the influenza virus H1N1 [76]. A small study revealed that montmorillonite particulate nanosilicate surface-modified platelets containing silver nanoparticles that shows antiviral efficacy against influenza A virus [76].

Given the material's stability and bio-compatibility, the researchers additionally claimed a wide range of antiviral use for these NPs [76]. Tio2 NPs were studied in their anatase phase that demonstrated to suppress the H9N2 virus. It's worth noting that NPs activate in the occurrence of UV light had more hyperactive action than those that weren't. The antiviral activity of (Cu^{+2}/Ti_{O2}) NPs with higher photo-catalytic action was investigated. The results showed that they had

more antiviral activity than their titanium dioxide equivalents. When the UV intensity is 0.5mW/cm2, the quantity of H9N2 is 0.1ml, and the UV illumination time is 2.5 hours, the following results are obtained.period is 2.5h, the inactivating rate of H9N2 viruses may approach 100% [76].

In another work, Tio2 NPs electrostatically linked to DNA (v3') directed to the 3' end of viral (H3N2) DNA significantly limited virus multiplication [93]. Further research revealed that the DNA-tagged titanium dioxide NPs had a comparable effect next to H5N1 and H1N1 viruses [94]. Further intriguing research is calcium supplementation compound to inactivate influenza viruses. Within 5 seconds of incubation, scallop shell powder pulverised to nanoscale size has shown remarkable inactivation capability in addition to the avian influenza virus also Newcastle disease virus and goose parvovirus. The study found that calcium oxide, which has little action at 2m, at 550nm; it causes inhibiting activity [95]. In another study, calcium phosphate .

NPs mirrored vaccinations' capacity to generate a T-cell response. Bi-functional (containing viral antigen) NPs were capable to aim viruses specifically and elicit an immunological reaction that results in elimination eradication of contaminated cells from the systems [96]. These compostable NPs offer enormous potential as a revolutionary immunization technique with significant flexibility and broad application [97]. This has been addressed by zinc oxide's function NPs in with flu infection. Zinc oxide NPs have been proven to decrease the human pulmonary immune system and reduce macrophage reaction to pathogens, and so should not be used during flu pathogens [98].

Magnetic NPs tag with particular viral binding agents has been proven in recent research to be useful in extreme gradients magnetic separation for medicinal purposes hemo-filtration [99]. This cutting-edge, developing technology, in which human blood is clean by magnetic matter labeled with vector of interest, has significant assure in the fields of remedial and virology assays

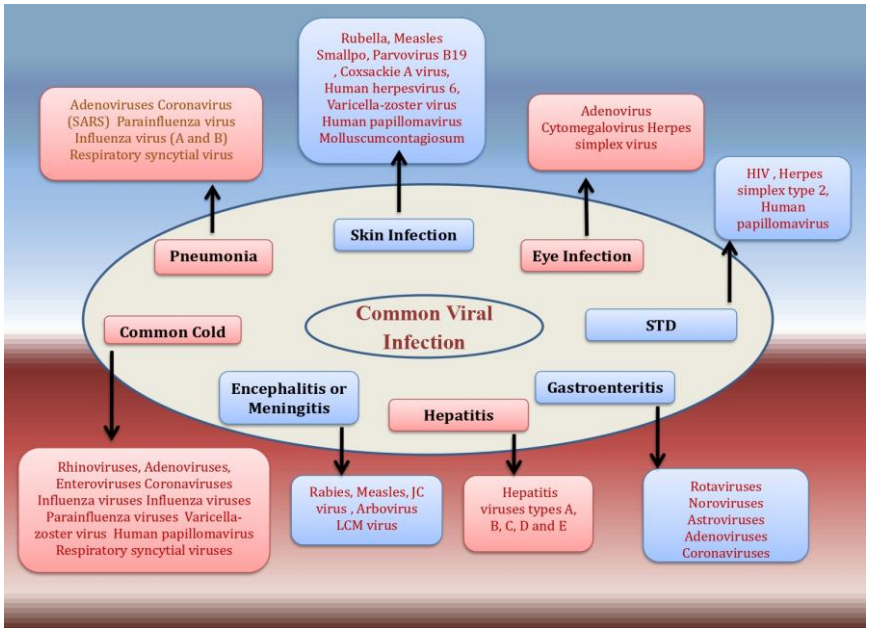

Figure 3: Types of common viral infections.

4. Antiviral mechanism in viral infection

Current outbreak of an acute infection cause by a novel emerging virulent pathogen that has evolved confrontation to existing anti-viral medications have prompted many researchers to look for new antiviral treatments. The viral illness is depending on the virus's capabilities ability to enter and connect through the host cells viral surface components bound to proteins and ligands on the cell membrane. The greatest procedure for creating new antiviral medication are being developed disrupt the connections between the virus receptor and the cell membrane, preventing the virus from attaching to and entering the cells. After researchers studied the method of operation of metal NPs in microorganisms, (AgNPs) have emerged as among the most capable antiviral possibilities. Microbes' resistance to AgNPs has been proven due to the extensive assault ranges of these NPs figure [4].

AgNP's mechanism of action against virus. The effects of AgNPs on viruses have been studied in a variety of ways. The interaction's specifics, however, are restricted. The complexity of viral structures contribute to the lack of comprehension of NPs' antiviral mechanisms. AgNP interacts with the harmful virus in two ways: (1) it adheres to the virus's external layer and prevents it from spreading. virus attachment to cell receptors; (2) it binds to the virus's DNA or RNA, reducing virus reproduction or propagation inside the cells of host. Antiviral effects of AgNPs against many pathogenic viruses. Understanding how these NPs work is important against various types of viruses might lead to the development of novel viral therapies employing nanotechnologies figure [5] [112].

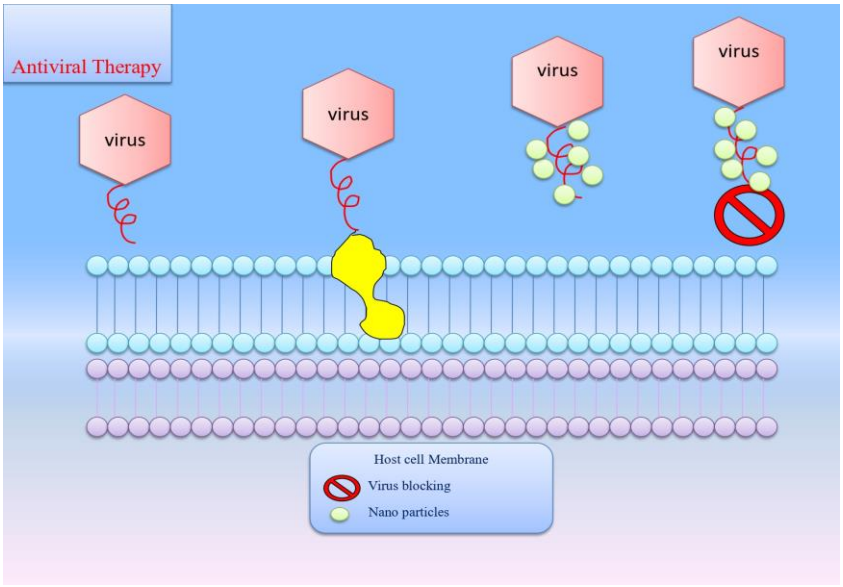

Figure 4: Antiviral treatment based on NPs. The entrance the virus's technique into the host cell is a popular target for antiviral treatment. One can drastically restrict virus entrance into a via electrostatically inhibiting viral receptors (on the virus or on the host cell), thus suppressing viral infection.

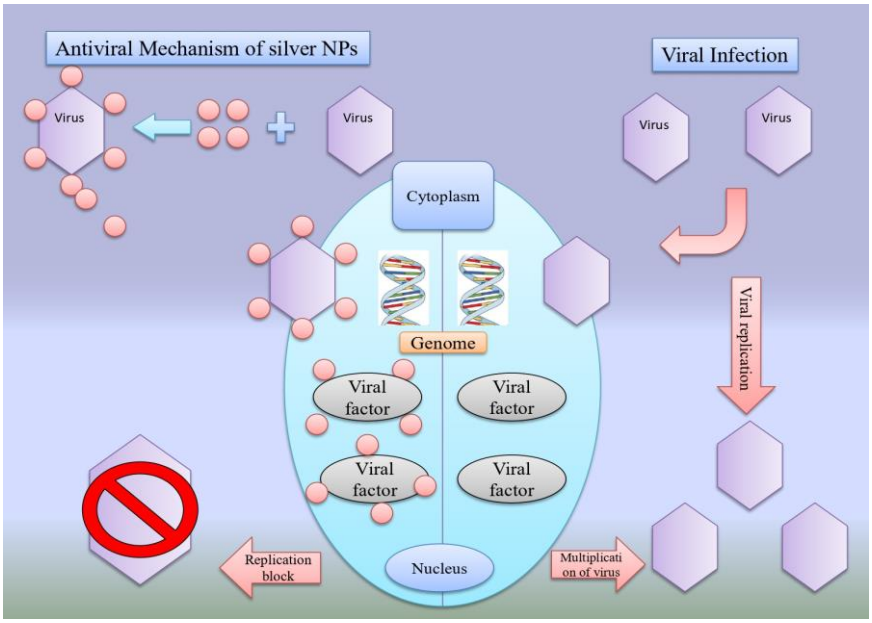

Figure 5: The antiviral activities of silver NPs.

Table 1: Various types of viruses their mechanism, vaccine and company.

Virus	Mechanism of action	Vaccine	Company	Name	Approval year/ stage of development	Reference
Influenza	Liposomes imitate the structure of endogenous viruses, enabling for cellular antigen presentation. membrane fusion and entrance Maintaining the natural appearance antigens on the surface of liposomes ensures a high level of immunogenicity	Virosomal (150 nm liposomes) vaccine	Crucell, Berna Biotech	Inflexal V®	1997	Herzog *et al.*,100 Mischler and Metcalfe,101 Bachmann and Jennings102
HAV	Unique reaction method that replicates the natural process	Inactivated virosomal (liposome) vaccine	Crucell, Berna Biotech	Epaxal®	1999	Bovier103
HCV	enhanced stability of protein through PEGylation	PEGylated-interferon alfa-2b	Merck	PegIntron®	2001	Alconcel *et al.*104
HBV,HCV	enhanced stability of protein through PEGylation	PEGylated-interferon alfa-2b	Genentech	Pegasys®	2002	Alconcel *et al.*104
Influenza	Containing influenza surface proteins neuraminidase and hemagglutinin	Virosome vaccine	Solvay pharma/Abbott	Influvac® Plus	2005	Waknine105
H5N1 and H1N1 influenz	Gene silencing	Short interfering RNA (SiRNA) therapeutic	Sirnaomics Inc.	FluquitTM (STP 702)	Preclinical evaluation	Sirnaomics106
HPV	Gene silencing	Short interfering RNA (SiRNA) therapeutic	Sirnaomics Inc.	FluquitTM (STP 702)	Preclinical evaluation	Sirnaomics106
HIV, HSV	Dendrimer derived lysine and including naphthalene disulfonic acid surface groups	Dendrimer	Starpharma	VivaGel® (SPL 7013)	Clinical trial used against bacterial vaginosis)	Starpharma107
HIV	The HIV-specific precursor/memory T cell pool was significantly expanded by a synthetic plasmid DNA immunogen encoding 15 antigens.	Theraputic vaccine	Genetic Immunity	DermaVir	Clinical trial (number NCT00270205	Rodriguez *et al.*108
HIV	Non-nucleoside reverse transcriptase Inhibitor	Solid drug NP Formulation	Merck	Doravirine (MK-1439)	Clinical trial (number: NCT02549040)	Molina *et al.*109
HVB	Three RNAi therapies targeting three locations on the HBV genome are contained in a lipid particle.	Wet lipid NP	Arbutus Biopharma	ARB-001467 TKM-HBV	Clinical trial (number: NCT02631096)	Seto *et al.*110

4.1 Nanovaccine

Nanovaccines are a subgroup of vaccinations designed to fine-tune the immunological response of the patient. They are among the few antiviral medicines that target the host. Due to their amount, form, utility and surface makeup, nanovaccines can overcome challenges caused by regular vaccinations. Currently, the danger of

pathogens returning to an immunogenic state of virulence limits live-attenuated vaccinations. While some vaccinations use inactivated viruses to reduce the danger, this results in a lower immune response. Due to significant qualities [111], nanovaccines can rise above these problems and act over a broad range of immunity figure [6].

Antigens are also added into the NPs via conjugation or encapsulated. The nanovaccine preserves the antigen's fundamental structure, allowing it to remain in immune cells for longer. Because of the nanostructure, the vaccinations can be administered by intravenous, percutaneous or intranasal methods. A number of NPs have been conceived and developed as nanovaccines. With the goal of enhancing humoral and cellular immune resistance to infectious diseases Protein-based, phos-pholipid, polymers, carbon-based, inorganic, metallic nanomaterials are being investigated on the nanoscale for the creation of these vaccines. They've had their surfaces altered to contain vaccination antigen or develop epitomes to address antigen-presenting cells Sulphide or thiolate gold chemistry has showed promise in metallic systems encouraging findings in terms of antigenic epitope presentation table (1) [111].

There is also some mention of research towards nanovaccines with several functions. The oil exact structure is efficient in loading molecules with chitosan membrane was created to provide a single dose of immunization with a prolonged time of immunoprotection using Hepatitis B surface antigens. The chitosan nanocapsules with a positively charged surface had a stronger reaction of the immune system and longer-lasting effect on hepatitis B. When thawing and rehydrating for vaccination, the structure was frozen and dried to provide a vaccination that is stable and longer shelf life with physic-chemical recovery features [111].

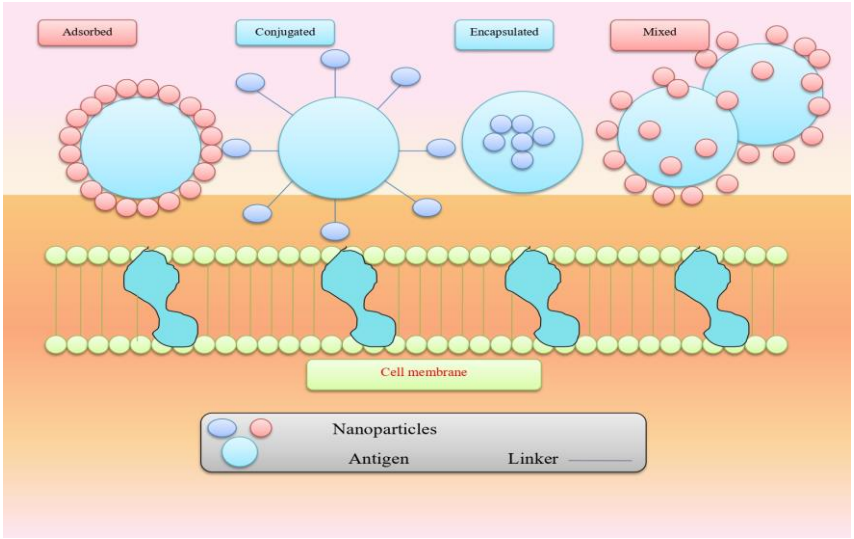

Figure 6: Design of Nanovaccine.

Table 2: Vaccine delivery systems based on nanocarriers and NPs against viral infections.

Disease	Virus	Antigen/Adjuvant	Nanocarriers Delivery System	Administration Pathway	Refs.
HIV/AIDS pandemic	HIV-1	DNA from viral plasmids	AuNPs	Intradermal	29
Influenza	H1N1	CpG/M2e Membrane Matrix Protein 2 (M2e)	AuNPs	Intradermal	30
Foot and mouth disease	FNDV[a]	Viral protein	AuNPs	Intradermal	31
Influenza	H1N1,H3N2,H5N1	M2e/CpG	AuNPs	Intranasal	32
Hepatitis B	HBV[b]	HBsAG	Chitosan NPs	Intraperitoneal	33
-	-	Hen egg lysozyme	Carbon magnetic NPs	Intravenous	34
Newcastel disease	NV[c]	Liver virus vaccine	Chitosan NPs	Intranasal or oral	35
Hepatitis B	HBV	HBsAG	PCL[d] / chitosan NPs	Intranasal	
Influnza	H1N1	Hemagglutinin (HA)	γ-PGA NPs	Intranasal	36
Norwalk virus	NV	Capsid protein	VLPs	Oral	37

infection					
Hepatitis	HBV	Nucleocapsis protein	VLPs	Intravenous	38
Influenza	H3N2	Structural protein, eg, HA, Neuraminidase, Na, and matrix (MI)	VLPs	Intramuscular	39
Rota virus	RV[e] 8-2/6/7-VLP	Cholera toxin (CT) and E.coli toxin are two examples of proteins.	VLPs	Rectal	40
SARS-CoV	CoV	Viral protein (spike)	Polypeptide NPs	-	41
Hepatitis B	HBV	HBsAg	Alginate coated chitosan NPs	Intranasal	43
Hepatitis B	HBV	Hepatitis B surface antigen	PLA and PLGA NPs	Pulmonary or intramuscular	44
Tetanus	TT f	Tetanus toxoid	PLA and PLGA nano/micropraticles	Intramuscular	45
Bovine respiratory	BPI3V g	BPI3V proteins	PLGA NPs	Intranasal	46
Bovine respiratory syncytial	RSV	F and G glycoproteins	Polyanhydride	Intranasal	47
RSV, influenza, HIV-1	RSV	TLR-7/8 agonist F protein	HPMA/NIPAM h	Intramuscular, intranasal, intravenous	48-49
Influenza	H1N1	trehalose 6,60 dimycolate, M2, HA, NP/MPL j	DLPC i liposomes	Intramuscular, intratracheal, intranasal	50
HIV/AIDS	HIV-1	PSA/mRNA encoding	Cationic nanomicelles based on PSA k	-	51

5. Conclusion and Future perspectives

As a result, NP-based delivery methods provide different possibilities to overcome obstacles associated with traditional therapeutic treatments, and as a result, they have attracted the attention of many researchers in the treatment of viral outbreaks. Because so many viral diseases are subclinical, early diagnosis and treatment of symptoms to reduce the severity of illness would have been extremely advantageous in preventing the spread of the virus. This is obviously a potential instrument for scientific research and therapeutic application. When compared to conventional approaches, modern development in nanomedicine potential to encompass or integrate medication with surface treatment, medication distribution systems intracellularly or to specific groups of cells, bio-compatibility, capacity to attain sluggish and prolonged drugs distribution offer higher remedial effects.

These changes can help overcome some of the most typical drawbacks of NPs in biological applications, such as higher permeability of biological membranes and related specific absorption, as well as lower toxicological profiles. The use of "nanotraps" has shown that influenza viruses may be effectively inhibited. By selectively changing the extra carbohydrates of the designated host receptors, this may be applied to additional infections like Aids, liver disease, and others. Further study and development of these particles is necessary to achieve this goal. Furthermore, research into the post and production of anti-PEG antibodies, as well as the effects of PEGlated nano therapeutics, needs intense examination. The use of nanotechnology in the treatment of various diseases has enormous possible for enhancing the mechanism of action at present available medications or generating innovative drugs, each one is greatly required in sensitivity to drugs. In spite of varieties of advantages that NPs have over traditional pharmaceuticals, further study on the toxicity and hidden detrimental impacts of specific nanosystems has always been required.

Finally, nanotechnology is an important factor to control and eliminate the viral infection. They have a capability to induce the viral infection because of nanosphere, nanocapsule and nanotraps for preventing and control the virus. For the future perspective way, they have the capability to kill the virus directly and it is very cost effective. Therefore, nanomedicine might helpful for all the other infection.

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