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Review Article

A Critical Review on Nanoscience Advancement: In Treatment of Viral Infection

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Abstract

Viral contaminations speak to a general medical issue and one of the main sources of worldwide mortality. A large portion of the antiviral medications have low permeability, low dissolvability and other related physical properties which make them less efficient for the antiviral treatment. To conquer these constraints, different nanomedicine stages have been planned. Nanomaterials offer special physico-chemical properties that have various advantages for medicate conveyance as perfect devices for viral treatment. This review focuses on the currently used medicines used in viral infection, presents a broad overview of the application of nanosized materials for the treatment of common viral infections and shed light on the potential of nanotechnology to provide more effective treatment for HIV, Herpes simplex virus, Influenza virus and Hepatitis C virus. The action of antiviral medications could be improved with nanomedicine formulations. As the physicochemical properties of nanocarriers can empower their capacity to target the specific sites. When it comes to structuring nanocarriers, size is the most important factor and the nanoparticles can permit the controlled delivery kinetics, enhanced bioavailability, altered pharmacokinetics, and less side effects. Nanocarriers that build them appealing candidates for antiviral drug such as Improves bioavailability of the encapsulated actives, controlled release, reduce the toxicity associated with the anti-viral drugs. One of the important physicochemical properties mainly size is the most important design factor for nanocarriers for anti-viral drug delivery to the specific sites. Nanobased drug delivery also leads to enhance the potential of currently approved antiviral drugs.

Keywords: Nanotechnology, HIV, Hepatits virus, Influenza, HSV

INTRODUCTION

Viral infections occur because of the expansion of harmful viruses within the body. They act by the process of replication and killing the host cells or by attacking inertly inside the host cell for a while. They utilize the host cell to increase the production of different viral infections within the body[1]. Infectious agents, for example, microscopic organisms, infections, growths and parasites represent roughly 15 million passing around the world, with intense respiratory diseases and human immunodeficiency infection (HIV) being the main sources[2]. By 1990, only 5 medications had been authorized as antiviral specialists, though roughly 20 years after the fact more than 40 were available. The greater part of these specialists were created for the treatment of HIV infection[3], though others were dynamic against different herpes viruses (herpes simplex infection [HSV], Varicella zoster infection [VZV] and human cytomegalovirus [HCMV]), flu A and B infections, and hepatitis B and C infections. In 2009, the worldwide marketplace for antiviral medication reached total sales of roughly USD 28 billion. Trading of antivirals extended by 20% from 2004 to 2006, and a proceeding growth trend has been calculated till 2011.[4] Various natural product having very potential benefit in treatment of viral infection like Green tea, amla, aloevera, neem, navagraha plants etc.[94,95,100]

The development of safe and effective antiviral drugs is a complex and difficult task[5].

- Infections are intracellular parasites that rely entirely on the host cell's biosynthetic system to produce a variety of components such as membranes, proteins, and nucleic acids. Therefore, just a few number of infections explicit metabolic capacities can be focused by antiviral agents without hurting the host simultaneously.
- The antiviral medications have restricted dissolvability in aqueous media, short half-life time, and additionally moderate take-up by the body, low bioavailability when given in a ordinary dosage forms.

SCOPE OF NANOASPECT IN ANTI-VIRAL

- Nanotechnological procedures can be utilized to upgrade the design, technique and transport of antiviral medications.
- This relatively new class of nanomaterials, also known as nanopharmaceuticals, exhibits extraordinary properties as a result of their small size, disproportionate surface-to-volume proportions, and adaptable surfaces.
- It has been shown that nanoparticles can contain biomimetic properties, which bring about the antiviral properties. For example such as - silver nanoparticles and dendrimers.
- Property of nano size and controlled hydrophobicity/lipophilicity, such antiviral nanocarriers can target medications to specific tissues or organs.
- With regard to intravenous administration, possess the property of small size, nanoparticles can flow in the circulatory system without being held by the pulmonary vessels or taken-up by the reticolo-endothelial systems.(RES)[7].
- Nanocarriers can be created to enhance their ability to reach extracellular or intracellular sites, as well as to fight with viruses for cell surface receptor connections, both of which are important factors in regulating viral infections and overcoming medication resistance[7].

VARIOUS VIRUSES: TYPES, CURRENT MARKETED THERAPY

Infections are the main sources of disease and death around the world. These are the sub-microscopic intracellular parasitic particles of hereditary material contained in a protein coat, absolutely subordinate by host for cell replication, indicating both living and non-living qualities[8]. Many serious diseases, such as acquired immunodeficiency syndrome (AIDS), H1N1 influenza, H5N1 influenza, avian influenza, hepatitis B and C, and severe acute respiratory syndrome (SARS) are caused by viruses.

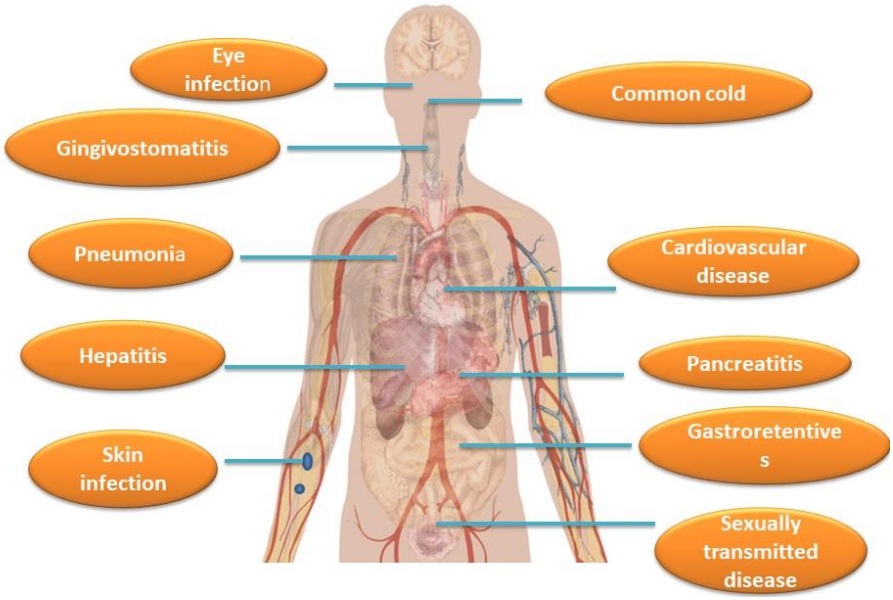

Figure 1: The above figure showing the various viral infections in the human body which are caused by a various viruses. Viruses can affect numerous areas in the body, such as the respiratory, reproductive and gastrointestinal systems. They can likewise affect the liver, brain and skin.

Table 1: The various viruses which are responsible for the human viral infections such as common cold, pneumonia, Hepatitis, skin infections etc.

Viral infections	Virus	Ref
Common cold	Rhinovirus, respiratory syncytial virus	[9]
Eye infection	Adenovirus, Herpes simplex virus ,zoster virus	[10]
Pneumonia	Influenza virus A, B, adenovirus, SARS coronavirus	[11]
Hepatitis	Hepatitis virus types A, B, C, D, E	[12,13,14,15]
Skin infection	Varicella zoster virus, smallpox, rubella, measles	[16]
Cardiovascular	Coxsackie B virus	[17]
Pancreatitis	Hepatotropic virus, Coxsackie virus, cytomegalovirus (CMV), human immunodeficiency virus (HIV), herpes simplex virus (HSV), mumps, varicella-zoster virus	[18]
Gastroretentives	Adenovirus, rotavirus	[19]
Sexually transmitted disease	herpes simplex virus type 1 or herpes simplex virus type 2,human papillomavirus, HIV	[20]

We will overview the five most broadly examined infections liable for a variety of clinical manifestations: Hepatitis B virus, Influenza virus, human immunodeficiency virus (HIV), hepatitis C virus (HCV) and Herpes simplex virus and their current marketed drugs-

HEPATITIS B VIRUS

Hepatitis B infection (HBV) contaminates in excess of 300 million individuals worldwide and is a typical reason for liver cancer and liver disease[21]. It belongs to the family *Hepadnaviridae* and it is a small, enveloped virus with a double-stranded DNA genome approximately 3.2 kb in size[22]. HBV imitates through a RNA intermediate which is also termed as retrotransponses is a type of hereditary segment that can incorporate into the host genome by changing over RNA again into DNA. The one of a kind highlights of the HBV replication cycle present a capacity of the virus to persevere in infected cells. The FDA (Food and Drug Administration) of the United States has approved seven medications for the treatment of HBV are interferon-alpha and pegylated interferon-alpha, two nucleotide analog prodrugs and three nucleoside analogs[23] which are shown in table 2 .

An examination indicated that the obstruction rate was as high as 70% after 5 years of lamivudine (LAM) treatment[24].Long-term utilization of adefovir dipivoxil can harm renal capacity, and telbivudine can expand creatine kinase levels, prompting muscle pain. The NAs with high obstructions to resistance, for example, entecavir (ETV) and tenofovir disoproxil fumarate (TDF), have essentially diminished medication resistance. The patients who use ETV or TDF have great virologic reactions, but drug safety also plays a vital role in deciding which drug should be given to a patient.

INFLUENZA VIRUS

It belongs to the family *Orthomuxoviridae* and influenza viruses are enveloped negative-strand RNA viruses, with segmented RNA genome possess 8 to 7 segments[25] and it is the most common cause of human respiratory infections .Influenza virus, as an enveloped virus, can survive for several hours depending on environmental circumstances (e.g. humidity and temperature), and it can survive longer (up to several months) in water at low temperatures (e.g. 20 °C)[26].It is an intense respiratory illness portrayed in its full structure by the unexpected beginning of high fever, coryza, migraine, cough, discomfort, and inflammmation of the upper respiratory tract and trachea. The main medications authorized for influenza avoidance and control are the adamantane derivatives (M2 inhibitors) rimantadine and amantadine and the neuraminidase inhibitors (NAIs) oseltamivir, zanamivir (utilized worldwide) shown in table 2.

The drug Zanamivir having the poor oral bioavailability (approximately 2%), so it is administered by inhalation. However, the inhalation route is not recommended in patients with chronic respiratory conditions. Different approaches to increasing the oral bioavailability of zanamivir have been studied[27]. For example a study has been done by Cao et al. prepared Zanamivir-loaded SLNs, which having the high entrapment efficiency, prepared by the double emulsion solvent evaporation method, which we will discuss in the nanoaspects of influenza virus[28].

HERPES SIMPLEX VIRUS

Herpes simplex virus (HSV) is a virus species that belongs to the *Herpesviridae* family, the *Alphaherpesvirinae* subfamily, the *Simplexvirusgenus*[29] and includes HSV1 and HSV2, which are responsible for the pandemics of various herpes. Herpes simplex type 1 virus (HSV-1) is a neurotropical double-stranded DNA virus that causes cold sores, keratitis, and sometimes human encephalitis. HSV is spread from person to person through direct contact with contaminated secretions. During viral contaminations, the incubation time of HSV-1 or HSV-2 is 4 days (extend, 2 to 12 days). HSV-1 for the most part causes pneumonia, encephalitis, or orofacial rankles, or keratitis, while HSV-2 ordinarily causes meningitis or genital sores[30].

Several drugs have been licenced for the treatment of HSV Some commonly known anti-herpetic drugs that are currently being used include acyclovir (ACV), penciclovir, Valacyclovir and famciclovir, which inhibit HSV-1 and HSV-2 infection by interfering with the viral DNA polymerase and hence, viral genome replication are shown in above table 2 .Acyclovir (ACV) is the medication of decision for HSV diseases. In any case, because of its short half-life and inadequate absorption it must be taken by oral dosage forms by multiple times day by day (up to 1200 mg/day), and the dose stretch for intravenous is 8 h.

The fundamental explanation is that Acyclovir is a class III medication as per the Biopharmaceutics Classification System: it is marginally solvent in water has a short plasma half-life, its ingestion from gastrointestinal tract is moderate and incomplete, and oral bioavailability ranges from just 10% to 30%. As an outcome, higher doses are recommended, resulted in adverse and systemic[31] so nanomedicines of ACV are increasing more significance.

HEPATITIS C VIRUS

HCV belong to the *Flaviviridae* family is a enveloped, small and positive single -stranded RNA virus which is discovered in 1989,it is a significant blood borne human pathogen. It is a significant reason for liver cirrhosis and hepatocellular carcinoma[32]. HCV transmission principally occured through contaminated blood and blood items transfusion, infusion medicates use, hemodialysis and organ transplantation; anyway unprotected sex and birth from a contaminated mother have likewise been archived as different methods of transmission[33]. The FDA approved drugs for HCV are appeared in above table 2. HCV was treated with pegylated-interferon (PEG-IFN) alpha in addition to ribavirin (RBV) allowed for 24 weeks or 48 weeks. In 2011, the main direct-acting antiviral medications (DAAs), telaprevir and boceprevir, were affirmed by the United States Food and Drug Administration (FDA). Concerning focusing on liver targeting of hepatitis medicines so nanocarriers can use to diminishing their harmful impacts in different tissues, improving medication viability and decreasing administration frequency, with resulting increments in patient compliance, and some are discussed below in nanocarriers for HCV.

Table 2: Approved Anti-viral drugs by FDA for HBV, Influenza, HSV and HCV treatment and their route of administration

Virus	Anti-viral drugs	Route of administration	FDA approval	Ref
HBV	Pegylated interferonalpha-2a		2005	[34]
(Interferons)	Pegylated interferon alpha-2b	Subcutaneous	1992	
(nucleotideanalog prodrug)	Adefovir, dipivoxil	Oral	2002	[35]
	Tenofovir, disoproxil fumarate	Oral	2008	
(nucleoside analogs)	Lamivudine	Oral	1998	[36]
	Entecavir	Oral	2005	
	Telbivudine	Oral	2006	
Influenza virus	**M2 inhibitors-**			[37]
	Amantadine	Oral	1996	
	Rimantadine	Oral	1993	
(NAIs)	Oseltamivir	Oral	1999	[38]
	Zanamivir	Inhalation	1999	
	Peramivir	Intravenous	2014	
	Laninamivir	Inhalation	2010	
HSV	Acyclovir	Oral,topical, I.V.	1982	[39]
	Famciclovir	Oral	1994	
	Penciclovir	Topical agent	1996	
	Valacyclovir	Oral	1995	
	Docosanol	Topical agent	2000	
HCV	**NS3/4A inhibitors(protease inhibitors)**			[40]
	Boceprevir	Oral	2011	
	Telaprevir	Oral	2011	
	Simeprevir	Oral	2013	
	Asunaprevir	Oral	2014	
	Grazoprevir	Oral	2016	
	Paritaprevir	Oral	2014	
NS5Ainhibitors	Ombitasvir	Oral		[40]
	Ledipasvir	Oral		
	Daclatasvir	Oral		
	Elbasvir	Oral		
	Velpatasvir	Oral		
NS_5B inhibitors	Sofosbuvir	Oral		[40]
	Dasabuvir	Oral		
Interferons	Interferon alfacon 1	Subcutaneous	1997	[40]
	Pegylated interferon Alfa 2b	Subcutaneous	1986	
	Pegylated interferon Alfa 2a	subcutaneous	2002	

HIV

The two lentiviruses, which are human immunodeficiency viruses types 1 and 2 (HIV-1 and HIV-2) are the main causative agents of Acquired immunodeficiency syndrome (AIDS) of humans[41]. A retrovirus, presently named human immunodeficiency infection type 1 (HIV-1), is one of the most pulverizing disease to have developed in late history.

Antiretroviral therapy (ART) is a combination of drugs which are used to treat HIV which are administered orally once or twice a day. The first drug, approved by the US FDA in 1987 is zidovudine, and about 25 medications have been approved to date, which is shown in table 3, many of which are also available in generic formulations and fixed-dose combinations and include six classes of drugs, i.e, nucleoside/nucleotide reverse transcriptase inhibitors, non-nucleoside inhibitors, entry/fusion inhibitors, protease inhibitors , integrase inhibitors and CCR_5 antagonists[42]**.** Only one anti-HIV drug, the oligopeptide, enfuvirtide, requires subcutaneous administration[43].Numerous difficulties occurred in destruction of HIV from contaminated cells like poor bioavailability of HIV drugs, achieving efficacious drug concentrations in viral reservoirs, drug resistance and systemic side effects, drug–drug interactions, poor patient compliance. To overcome these problems, different ART nanodelivery approaches have been developed in the last several decades which have been described in the reviews which we discussed in nanocarriers used in anti-viral.

Table 3: FDA Approved Anti-viral drug for the treatment of HIV

Anti-viral drugs	Route of administration	FDA approval	Ref
NNRTI			[44]
Nevirapine	Oral	2011	
Delavirdine	Oral	1997	
Efavirenz	Oral	1998	
Etravirine	Oral	2008	
Rilpivirine	Oral	2011	
Intefrase Inhibitors			[45]
Raltegravir	Oral	2007	
Protease Inhibitors			[46]
Saquinavir	Oral	1995	
Indinavir	Oral	1996	
Ritonavir	Oral	1996	
Nelfinavir	Oral	1997	
Lopinavir	Oral	2000	
Amprenavir	Oral	1999	
Fosamprenavir	Oral	2003	
Atazanavir	Oral	2003	
Darunavir	Oral	2006	
Tipranavir	Oral	2005	
Fusion Inhibitors/entry			
Enfuvirtide (T20)	Subcutaneous	2003	
Maraviroc	Oral	2007	[47]
NRTI-			
Zidovudine	Oral	1987	
Didanosine	Oral	1991	
Zalcitabinea	Oral	1992	[47]
Stavudine	Oral	1994	
Lamivudine	Oral	1995	
Abacavir	Oral	1998	
Emtricitabine	Oral	2003	

Apart from changing formulations, another technique currently being explored to tackle viral infections is the creation of new nano-delivery systems for drug administration.

DESIGN OF NANOTECHNOLOGY IN ANTIVIRALS

Nanotechnology refers to the phenomenon or usefulness of particles of various dimensions (10–9 or one billionth of a meter) falling into the nanometer[48]. Nanoparticles may have a effect on the fate of the encapsulated drugs and rule it The primary nanosystem used in medicines were introduced to improve the potency of a new, yet dose limiting, and poorly bioavailable drugs[49]. The creation of new methods for achieving controlled release is therefore a very promising research field, both in terms of the need to improve healthcare and from the perspective of pharmaceutical companies in retaining sales and in securing patent positions in existing and new medicines.

The eventful benefits of nanocarriers that build them appealing candidates for antiviral drug supply are[50]:

- Improves bioavailability of the encapsulated actives
- Controlled release
- Reduce the toxicity associated with the anti viral drugs
- Improves therapeutic compliance
- Specific targeting
- Over cone the anatomical barriers

Intrestingly, formulation of nanocarriers may alter the physicochemical properties of most of molecules, thereby allows for sustained/controlled release, modified pharmacokinetics and focusing on particular network of action. It can lead to the improvement in drug efficacy and a reduction with a possible negative effect[51].

NANOCARRIERS

Nanotechnology is growing rapidly in the delivery of antiviral drugs, and it is becoming a significant point of research today. Nanomedicines are ready to promote the delivery of medication to the central system. 3 classes of nanocarriers are investigated for the delivery of antiretrovirals to the central nervous system: polymer/dendrimer-based, lipid-based and micelle-based systems[52]. Nanocarriers for oral nanoformulations ought to be proof against the acidic pH scale of abdomen and enteral enzymes, and be able to penetrate the mucous secretion that limits the intestinal presence of those medication. Now examples of various biocompatible systems are discussed.

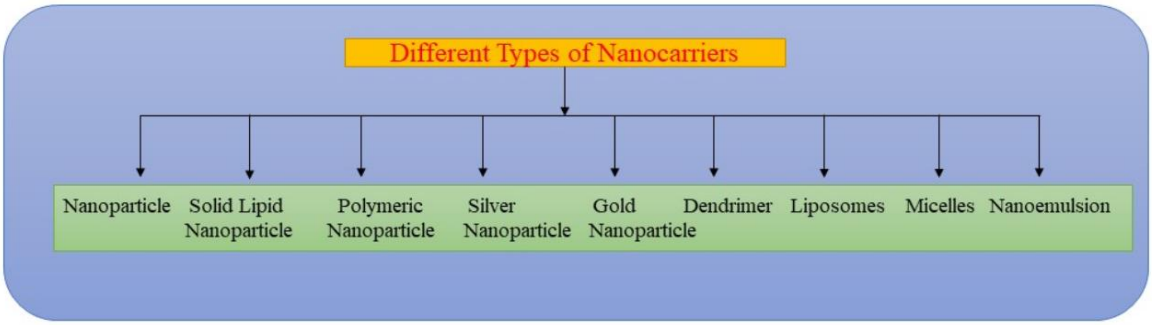

Figure 2: Different types of Biocompatible Systems to enhance the bioavailability and for specific targeting at a site of action

NANOPARTICLES

Nanoparticles are stable colloidal particles having size <1 micrometer in diameter and will be created the usage of polymers, lipids, proteins or different substances, together with inorganic materials. Because of their tiny sizes they will be administered intravenously[53].The various nanoparticle are as follows-

POLYMERIC NANOPARTICLE

Polymers are used to form the polymeric nanoparticle that may fall under any of the accompanying classes: synthetic homopolymers, colloid stabilizers, copolymers, natural polymer[54]. Most commonly used polymeric nanoparticles are of poly-d l-lactide-co-glycolide (PLGA), poly-ε caprolactone, poly-alkyl-cyanoacrylates, poly-(γ-glutamic acid) (γ-PGA), polymethylmethacrylate (PMMA), polyvinylpyridine, polyacrylamides, polyethyleneimine (PEI), polygluteraldehyde, human serum albumin (HSA), gelatin and chitosan[55].

SOLID LIPID NANOPARTICLES

Introduced within the starting of the 1990s, solid lipid nanoparticles (SLNs) are the nano scaled moieties made up of lipids. They're stabilized with the utilization of emulsifiers and co-emulsifiers, such as polysorbates, poloxamers, fatty acid co-esters, bile salts and lecithin. They have been profitable in delivering molecules to the BBB and different viral reservoirs like delivery of Atazinavir which is encapsulated in SLNs to the human brain endothelial cell line. The foremost likely route of Transport of such systems is receptor mediated endocytosis[56].

SILVER NANOPARTICLES

Silver nanoparticles are the best of the metallic nanoparticles against microscopic organisms, eukaryotic microorganisms, viruses especially due to the inalienable inhibitory and bactericidal capability of silver[57].A few investigations demonstrated antiviral capability of the silver nanoparticles. Ag+ particles discharged from silver nanoparticles connect legitimately with biomolecules that contain phosphorus or sulfur, including proteins, DNAs, and RNAs. It appears that silver nanoparticles interfere with a few phases of the viral replication cycle including the connection of the virus to the cell membrane and their entrance into the cells, DNA and RNA replication, and protein synthesis. Elichegurra et al. were the first to exhibit the impact of silver nanoparticles (Ag NPs) on HCV-1[58].

GOLD NANOPARTICLES

Gold nanoparticles (GNPs) are broadly investigate as nanocarriers because of their magnificent conductivity, biocompatibility, adaptability of surface adjustment and simple preparation techniques[59] in certain discoveries, that too when, AuNPs offset with certain biocompatible polymer could go about as an effective antiviral specialists against HIV-1, H1N1, H3N2, H5N1, dengue contamination, looseness of the bowels infection and Foot-and-mouth sickness contamination (FMSC)[60,61]. Also, AuNPs can go into various cell types, cross the blood–brain boundary (BBB) and apply antiviral movement upon conjugation with an antiretroviral.

DENDRIMER

Dendrimers are artificial polymers with three-dimensional, star-molded and a branched macromolecules[62]. Dendrimers have an outer layer that's dominated by useful functional groups for the conjugation of medicines and specializing in moieties[63]. The mix of maraviroc and tenofovir into the dendrimers showed a additional outstanding opposing HIV-1 activity than one medication. This drug delivery system has resolved most of the issues related to the drug like solubility, porosity, and drug loading. The only major drawback with this technique is that it interacts with the plasma membrane that makes it harmful as a carrier system.

LIPOSOMES

A liposome is a circular vesicle having one lipid bilayer and will likely be used as a vehicle for the administration of drugs[92]and also consist of aqueous layer having a size range of 20-30 nm[64]. They are able to encapsulate hydrophilic drugs within their inner aqueous phase and lipophilic drugs within their lipid bilayers.[93] Liposomal formulations for cancer therapy available on the market are DoxilR (pegylated liposomal doxorubicin; Ortho Biotech Products, Bridgewater, NJ, USA), MyocetR (non-pegylated liposomal doxorubicin; Cephalon, Frazer, PA, USA) and DaunoXome[65].

MICELLES

Micelles having a size range from 10 to 100 nm[66].They contain two regions which possess different affinities towards water, the core of the micelle is formed by hydrophobic fragment whereas the shell consist of hydrophillic fragment[67]. Drug encapsulation with compound micelles is one in every of the foremost fascinating nanotechnologies used to enhance every the water solubility and stability in the other case technologically restricted (poorly water soluble and unstable) medication[68].

NANAOEMULSIONS

Nanoemulsions are a colloidal particulate framework in the submicron size range acting as a transporter of medication particles contain oil, emulsifying agents, and aq. phase, they are additionally called as mini-emulsion which is fine oil/water or water/oil scattering balanced out by an interfacial film of surfactant molecules having size range 20–600 nm[69]. Nanoemulsions are potential tools for improving the oral bioavailability of poorly aqueous soluble drugs.

NANOFORMULATIONS AGAINST SPECIFIC VIRUSES

Now, we will discuss in a systematic manner the use of different nanomaterials for the treatment of viral infections. The focus will be on the three most widely investigated viruses responsible for a variety of clinical manifestations: human immunodeficiency virus (HIV), hepatitis C virus (HCV), Influenza virus and Herpes simplex virus.

HIV/AIDS is currently a worldwide pandemic that has become the main irresistible enemy of grown-ups around the world[70].The image below depicts various nanocarriers utilized in HIV treatment.

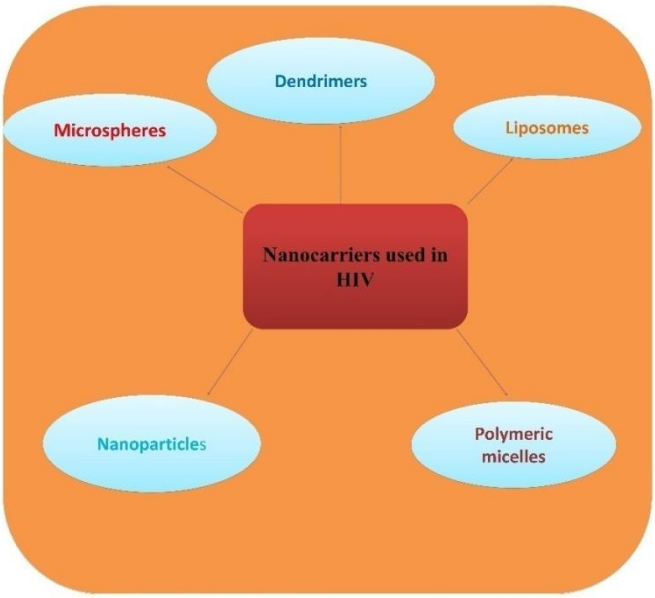

Figure 3: Nanocarriers used in HIV

Various studies has been done on liposomes as nanocarriers like the drug stavudine was encapsulated in liposomes (120–200 nm) and conjugated with mannose and galactose, leading to exaggerated cellular uptake compared with free drug or plain liposomes, and generating vital level of the drug in liver, spleen and lungs.

Chiodo *et al.* conducted an investigation. The NRTI drugs abacavir (ABC) and lamivudine (3TC) were appended to glucose-covered GNPs and assessed for their HIV action, in vitro. An functionalization was accomplished by means of the essential hydroxyl groups of the medications, through an ester bond that can be severed off in acidic conditions (for

example in the vagina to repress viral replication), to make the hydroxyl GRP accessible in order to promote chain termination - an important moa of the NRTI class of drugs .These outcomes outline another degree of multi-functionalization of GNPs as multivalent medication conveyance frameworks for the treatment of HIV[71].

Destache*et al.*[72] created PLGA NPs to simultaneously epitomize lopinavir, ritonavir and efavirenz, and assessed their phagocytosis into monocyte-inferred macrophages. The sustained release of medications from the PLGA nanocarrier affirmed scopes of antiretrovirals in cells till day 28 other than cytotoxicity. Besides, PLGA NPs have been analyzed for viability in vivo after intraperitoneal infusion in mice. The sustained release of the medications was once affirmed, as the nano-formulated antiretrovirals had been distinguished in blood and organs as long as 35 days after administered.

Jenita*et al.* have proposed albumin nanoparticles with efavirenz as an antiviral therapy. Efavirenz is an antiretroviral drug that inhibits HIV-1's non-nucleoside reverse transcriptase. The particles had a size of 250 nm and showed an entrapment effectiveness between 45%–72%; they expanded efavirenz conveyance into different organs by a few folds of extent in compared with the free drug[73].

Table 4: Available Nano-formulations for HIV

Nanoplatform	Name	Routeof administration	Inventor
Dendrimers	Viva Gel(SPL 7013 GEL)	Topically (vaginal gel)	Starpharma, Australia
Solid drug nanoparticle	Doravirine (MK-1439)	Orally	Merck
Therapeutic Vaccine	Dermavir	Topical administered	Genetic immunity
Liposomes	Combination of azidothymidine and lithium	Intravenous/rectal	Gabev and evgeni Bogomiloc (1998)
Micelles	Amprenavir or ritonavir	Oral	Abou Chacra-vernet et al. (2004)

HEPATITIS C VIRUS (HCV)

Because siRNA has a variety of difficulties, including low cell take-up, poor blood stability, and rapid nuclease breakdown[74], a large number of studies have used nanoparticles to address these challenges and limit the negative impact of "off-targeting.".

Lakshmi narayanan et al. utilized a galactose functionalized dendritic nanovector (DG) as a carrier for siRNA against the 5' untranslated locale of the HCV genome[75]. The siRNA-DG shaped a stable complex that had target-arranged conveyance through the interaction between its free galactose and asialoglycoprotein receptor. The conveyed siRNA located in the perinuclear area (the site of HCV replication) in which NS3 and NS5b viral proteins are co-restricted.

NANOPARTICLE AS A CARRIER FOR HCV VACCINE

Liu and partners[76] explored a technique to get IFNα-stacked nanoparticles good for the conservation of IFNα-2b biological functionality and integrity .The antiviral movement of the polysaccharide nanoparticles was demonstrated to be exceptionally saved (above 97%) both in vitro and in vivo. Li and colleagues encapsulated IFN-α into SLNs utilizing the double emulsion solvent evaporation strategy. Antiviral examines exhibited that SLNPs protected the bioactivity of IFN-α after encapsulation; for example it kept up its antiviral action.

Cross-connected polymeric micelles (CCPM) were utilized to target HCV, in vitro. The micelles were stacked with the recognized intense anti HCV compound, camptothecin (CPT)[77], which is additionally connected with constraints, for example, poor chemical stability and water solubility. The CLPMs utilized in this investigation formed an appropriate amphiphilic micelle containing a hydrophobic center and hydrophilic shell, which showed high loading capacity for CPT while keeping up HCV antiviral and lessen the cytotoxicity.

Table 5: Nanocarriers used in the HCV nanomedicines

Agents	Carriers used	Ref
Silibinin	Used as a liposomes	[78]
IFN –α	AuNP	[79]
Ribavarin	Polymeric micelles PLA/AG-PLLNPs PGA NP	 [80] [81]
DNAzyme to target HCV NS3 gene	MPAP/iron oxide NPs	[82]
HCV polymerase inhibitors and protease inhibitors	HCV protease and polymerase inhibitors + anti-fibrotic/anti-hemolytic + viral entry inhibitor agents + naturally driven polyphenol/thiols and non-anticoagulant GAGs	[83]

HERPES SIMPLEX VIRUS (HSV)

As we have seen above that higher doses are recommended, resulted in adverse and systemic, so nanomedicines of ACV is increasing more significance. Nanospheres were assessed as delivery agents for the buccal route of acyclovir with an end goal to expand bioavailability. In vivo investigations in bunnies demonstrated a increment in the retention of acyclovir-stacked nanospheres with top plasma concentration three crease higher than the free medication utilizing oral dosing. The outcomes likewise indicated that the greatest medication concentration was delayed (6 h versus 2 h), and this can decrease the recurrence of medication administration[84].Only a few materials exhibit anti-HSV action, according to recent research; gold and silver nanoparticles with sulfonate activities blocked viral entrance and stopped viral propagation from cell to cell.

Gold nanoparticles with the mercaptoethane -sulfonate 4 nm in size imitate heparin sulfate present on the host cell and thereby block HSV attachment to the cell and inhibit viral entry[85].

Szyma'nska *et al*. for example. A multifunctional tannic acid -modified silver nanoparticles -dependent mucoadhesive hydrogels has been developed to improve the local treatment of herpes simplex virus (HSV) infections[86]. On the vaginal mucosal surface, silver nanoparticles treated with tannic acid (TA -AgNPs) have been shown to effectively minimize the HSV-2 infectivity, indicating the possible use of functional nanoparticles as microbicides in HSV preventive. To further improve the antiviral efficiency of TA-AgNPs, a three-dimensional cross-linked polymer matrix was created to encapsulate TA-AgNPs and build a hydrogel, and the hydrogel formed of mucoadhesive polymers provided constant link in between drug carrier and the mucosal tissue, thereby enhancing TA-AgNPs efficacy.

As an ocular delivery system, solid lipid nanoparticles will play an important role. In 2013, two lipid formulations (i.e. solid lipid nanoparticles and nanostructured lipid carriers) were developed by Seyfoddin and colleagues[87] to boost the ocular bioavailability of ACV. The high efficiency of encapsulation, superior physical properties and better release profile from nanostructured lipid carries indicated that this formulation could be used as a potential ocular drug delivery system for ACV.

INFLUENZA VIRUS

Inputs from the Nanotechnology solutions against the anti-influenza, as gathered from the few reported available online are summarized below and summarized in table 6.

Table 6: Nano aspects against the Influenza virus

No.	Name	Type of nanotechnology	Virus	Ref
1.	Silver nanoparticle	Nanoparticle of 5-20nm	Influenza A {H1N1}virus	[88]
2.	TiO2 nanoparticle	Nanoparticle of 4-10nm	H3N2strain	[89]
3.	M2e-AuNanoparticle	Nanoparticle of 12nm	Influenza A virus	[90]
4.	Multivalent sialic acid,AuNP	Nanoparticle of 14 nm	Influenza Avirus	[91]
5.	ZnO-NP/PEG NP	Nanoparticle of 20-50nm/16-20 nm	H1N1 virus	[92]

Oral Ooeltamivir or inhaled zanamivir, are the essential drugs recommended for antiviral treatment. Zanamivir have low oral bioavailability (generally 2%), and it is given by inhalation route as we have inspected above. Along these, the route of inhalation isn't proposed in patients with endless respiratory conditions and it is in like manner difficult to figure out how to the pediatric children. Therefore, the progression of a novel oral plan that updates the systemic introduction of zanamivir would basically extend its clinical utility and offer elective treatment decisions to individuals in case of pandemic. So, different approaches have been done to increase the oral bioavailability of Zanamivir.

Analyses to examine the activity of silver nanoparticles against flu infection were performed. Xiang et al[89].Formulated silver nanoparticles with sizes shifting from 5 to 20 nm and test them with various viral infectivity hindrance measures, for example, (i) hemagglutination restraint (HAI) tests and embryo inoculation assays; (ii) a cytotoxicity test of silver nanoparticles in MDCK cells; (iii) hindrance of silver nanoparticles of H1N1 flu A infection; and (iv) transmission electron microscopy (TEM) investigation joined with a flow cytometry (FCM) test. Results from these examinations recommended that silver nanoparticles give protection against flu infection diseases without the danger of cell toxicities.

Papp *et al* 2010. Shows Multivalent sialic functionalized AuNPs of 14 nm repressed flu A infection contamination. As the binding of the viral combination protein HA to the host cell surface is interceded by sialic acid receptors, a multivalent connection with sialic acid functionalized AuNPs is required to restrain viral disease.

Ghaffari*et al*[92] assessed the antiviral activity of zinc oxide nanoparticles (ZnO-NPs) and PEGylated zinc oxide nanoparticles against H1N1 flu infection and anti -flu activity was dictated by $TCID_{50}$. The normal measurements of ZnO-NPs extended somewhere in the range of 20 and 50 nm, while the ZnO-PEG NPs were run from 16 to 20 nm. The outcomes demonstrated that PEGylated ZnO-NPs have a higher anti flu action alongside lower cytotoxicity contrasted with exposed ZnO-NPs, At the most elevated non-harmful concentration, the PEGylated and unPEGylatedZnO-NPs prompted hindrance rate of 94.6 and 52.2%.

Antiviral activity of titanium dioxide (TiO2) nanoparticles against influenza virus was reported by Mazurkova *et a*l. 2010[89]. They used TiCl4 to make TiO2 nanoparticles with a size of 4–10 nm and tested them against the H3N2 influenza virus strain cultured on chicken embryo suspension culture. Their electron microscopic observation showed that influenza virus was destroyed by titanium dioxide nanoparticles within 30 min of incubation. They also suggested that the virus inactivation properties of TiO2 nanoparticles might be based on the direct contact between nanoparticles and virus particles. To find out the mechanisms of the antiviral effect of the TiO_2 nanoparticles, they studied the effect of nanoparticles in different condition as in dark, under ultraviolet irradiation, and during daylight illumination. They found that the antiviral activity of TiO_2 nanoparticles against influenza virus was not dependent upon daylight illumination or ultraviolet illumination.

The feasibility of using M2e–AuNP conjugates with CpG as an adjuvant as a medium for the production of an influenza A vaccine was evaluated by Tao et al.[90] and also its ability to

protect against influenza A virus in a mouse challenge model. AuNPs ranging 12 nm were blended with uniform shape and size and conjugated with M2e using gold–thiol cooperation, and their analysis provides a promising platform as an antigen carrier for this poorly immunogenic peptide for immunization against influenza A viruses.M2e – AuNP integrates stimulation of M2e-explicit IgG antibodies that can perceive M2e and local M2 in flu A infections and shield mice from fatal disease with PR8 flu A and result demonstrated that Mice vaccinated with M2e-AuNP conjugates were only partially protected against lethal PR8 test, whereas mice receiving soluble CpG as an adjuvant were completely safe, in addition to M2e – AuNP. Another suitable dosage form like niosomes, phytosomes, cubosomes, transdermals needles also better opportunities to increases the bioavailability and other parameter like solubility, permeability of antiviral drugs.[96,97,98,99]

DISCUSSION

Various diseases occur by microbes likes bacteria, viruses and fungi etc. Microbes have ability to resist against various medicines which effective against microbes. These medicines have some problems during formulation due to high molecular weight, solubility of drugs other physiochemical parameters which produced less bioavailability. For resolve these problems various nanotechnology design now a day's which are very useful to increase absorption of drugs in the body against various microbes. All nano formulations have unique property i.e. particles size which very helpful to design factor for nanocarriers for anti -viral drug delivery to the specific sites. These formulations provide better future against microbes with effectiveness, increase bioavailability. Researchers mainly focused on these dosages form due to great bioavailability, easy formulated, less in cost and good future scope in this research area with showing good effective against diseases occurs by viruses and other microbes. The review concludes that design nano formulations best dosage for fulfill the requirements of antiviral drug delivery to the specific sites.

Conflict of Interest

The author declared no conflict of interest.

ABBREVEATIONS

HIV	Human immunodeficiency virus
HSV	Herpes simplex viruses
VZI	Varicella zoster infection
HCC	Hepatocellular carcinoma
CH	Chronic hepatitis
CHB	Chronic hepatitis b virus
ACV	Acyclovir
RES	Reticolo-endothelial systems
AIDS	Acquired immunodeficiency syndrome
HCV	Hepatitis c virus
LC	Liver cirrhosis
HBV	Hepatitis b virus
FDA	Food and drug administration
ETV	Entecavir
TDF	Tenofovir disoproxil fumarate
NAIs	Neuraminidase inhibitors
RNA	Ribonucleic acid
SLNs	Solid lipid nanoparticle
PEG-IFN	Pegylated-interferon
DAAs	Direct-acting antiviral medications
ART	Antiretroviral therapy
EFV	Efavirenz
NNRTI	Nucleoside/nucleotide reverse transcriptase inhibitors
PLGA	Poly-d l-lactide-co-glycolide
γ –PGA	Poly-(γ-glutamic acid)
PMMA	Polymethylmethacrylate
AG NPs	Silver nanoparticles
GNP	Gold nanoparticles
AuNPs	Gold nanoparticle
ABC	Abacavir
NRTI	Nucleotide reverse transcriptase inhibitors
CCR-5	C-c chemokine receptor
INFα	Interferon alpha
siRNA	Small interfering rna
DTC	Dotap
ND	Nanodiamond
GQD	Graphene quantum dots
TiO_2	Titanium dioxide
ZnO-NPs	Zinc oxide nanoparticles
RTI	Reverse transcriptase inhibitors

REFERENCES

1. Akbarzadeh A, Kafshdooz L, Razban Z, DastranjTbrizi A, Rasoulpour S, Khalilov R, Kavetskyy T, Saghfi S, Nasibova AN, Kaamyabi S, Kafshdooz T. An overview application of silver nanoparticles in inhibition of herpes simplex virus. Artif Cells NanomedBiotechnol. 2018; 46(2):263-267. doi: 10.1080/21691401.2017.1307208. Epub 2017 Apr 12. PMID: 28403676.
2. Singh L, Kruger HG, Maguire GEM, Govender T, Parboosing R. The role of nanotechnology in the treatment of viral infections. *Ther Adv Infect Dis*. 2017; 4(4):105-131. doi:10.1177/2049936117713593
3. Milroy D, Featherstone J. Antiviral market overview. Nat Rev Drug Discov. 2002 Jan; 1(1):11-2. doi: 10.1038/nrd709. PMID: 12119604.
4. Lembo D, Cavalli R. Nanoparticulate delivery systems for antiviral drugs. Antivir Chem Chemother. 2010; 21(2):53-70. doi: 10.3851/IMP1684. PMID: 21107015.
5. Szunerits S, Barras A, Khanal M, Pagneux Q, Boukherroub R. Nanostructures for the Inhibition of Viral Infections. Molecules. 2015 Aug 3; 20(8):14051-81. doi: 10.3390/molecules200814051. PMID: 26247927; PMCID: PMC6332336.
6. Szunerits S, Barras A, Khanal M, Pagneux Q, Boukherroub R. Nanostructures for the Inhibition of Viral Infections. Molecules. 2015 Aug 3; 20(8):14051-81. doi: 10.3390/molecules200814051. PMID: 26247927; PMCID: PMC6332336.
7. Lembo D, Donalisio M, Civra A, Argenziano M, Cavalli R. Nanomedicine formulations for the delivery of antiviral drugs: a promising solution for the treatment of viral infections. Expert Opin Drug Deliv. 2018 Jan; 15(1):93-114. doi: 10.1080/17425247.2017.1360863. Epub 2017 Aug 3. PMID: 28749739.
8. Van Regenmortel M.H.V. Genetics and Evolution of Infectious Disease. Elsevier; Amsterdam, The Netherlands: 2011. Virus Species, 3–19.
9. Heikkinen T, Järvinen A. The common cold. Lancet. 2003 Jan 4; 361(9351):51-9. doi: 10.1016/S0140-6736(03)12162-9. PMID: 12517470; PMCID: PMC7112468.
10. Watson S, Cabrera-Aguas M, Khoo P. Common eye infections. AustPrescr. 2018 Jun; 41(3):67-72. doi: 10.18773/austprescr.2018.016. Epub 2018 Jun 1. PMID: 29922000; PMCID: PMC6003010.
11. Ruuskanen O, Lahti E, Jennings LC, Murdoch DR. Viral pneumonia. Lancet. 2011 Apr 9; 377(9773):1264-75. doi: 10.1016/S0140-6736(10)61459-6. Epub 2011 Mar 22. PMID: 21435708; PMCID: PMC7138033.

12. Thuener J. Hepatitis A and B Infections. Prim Care. 2017 Dec; 44(4):621-629. doi: 10.1016/j.pop.2017.07.005. Epub 2017 Oct 5. PMID: 29132524.

13. Ahmad J. Hepatitis C. BMJ. 2017 Jul 6; 358:j2861. doi: 10.1136/bmj.j2861. PMID: 28684552.

14. Rizzetto M. Hepatitis D Virus: Introduction and Epidemiology. Cold Spring HarbPerspect Med. 2015 Jul 1; 5(7):a021576. doi: 10.1101/cshperspect.a021576. PMID: 26134842; PMCID: PMC4484953.

15. Khuroo MS, Khuroo MS, Khuroo NS. Hepatitis E: Discovery, global impact, control and cure. World J Gastroenterol. 2016 Aug 21; 22(31):7030-45. doi: 10.3748/wjg.v22.i31.7030. PMID: 27610014; PMCID: PMC4988308.

16. Cojocaru FD, Botezat D, Gardikiotis I, Uritu CM, Dodi G, Trandafir L, Rezus C, Rezus E, Tamba BI, Mihai CT. Nanomaterials Designed for Antiviral Drug Delivery Transport across Biological Barriers. Pharmaceutics. 2020 Feb 18; 12(2):171. doi: 10.3390/pharmaceutics12020171. PMID: 32085535; PMCID: PMC7076512.

17. Hékimian G, Combes A. Myocardites [Myocarditis]. Rev Med Interne. 2017 Aug; 38(8):531-538. French. doi: 10.1016/j.revmed.2016.12.022. Epub 2017 Feb 2. PMID: 28161113.

18. Rawla P, Sathyajit S. Bandaru ,Vellipuram AR.Review of infectious etiology of acute pancreatitis .Gastroenterol Res,2017 Jun 30; 10(3):153-158.

19. Eckardt AJ, Baumgart DC. Viral gastroenteritis in adults. Recent Pat Antiinfect Drug Discov. 2011 Jan; 6(1):54-63. doi: 10.2174/157489111794407877. PMID: 21210762.

20. Gilson RJ, Mindel A. Recent advances: Sexually transmitted infections. BMJ. 2001 May 12; 322(7295):1160-4. doi: 10.1136/bmj.322.7295.1160. PMID: 11348912; PMCID: PMC1120285.

21. Liang TJ. Hepatitis B: the virus and disease. Hepatology. 2009 May; 49(5 Suppl):S13-21. doi: 10.1002/hep.22881. PMID: 19399811; PMCID: PMC2809016.

22. Wu CC, Chen YS, Cao L, Chen XW, Lu MJ. Hepatitis B virus infection: Defective surface antigen expression and pathogenesis. World J Gastroenterol. 2018 Aug 21; 24(31):3488-3499. doi: 10.3748/wjg.v24.i31.3488. PMID: 30131655; PMCID: PMC6102499.

23. Keeffe EB, Marcellin P. New and emerging treatment of chronic hepatitis B. Clin Gastroenterol Hepatol. 2007 Mar;5(3):285-94. doi: 10.1016/j.cgh.2006.09.036. Epub 2007 Jan 9. PMID: 17218162.

24. Wu YL, Shen CL, Chen XY. Antiviral treatment for chronic hepatitis B: Safety, effectiveness, and prognosis. World J Clin Cases. 2019 Jul 26; 7(14):1784-1794. doi: 10.12998/wjcc.v7.i14.1784. PMID: 31417924; PMCID: PMC6692272.

25. Taubenberger JK, Morens DM. The pathology of influenza virus infections. Annu Rev Pathol. 2008; 3:499-522. doi: 10.1146/annurev.pathmechdis.3.121806.154316. PMID: 18039138; PMCID: PMC2504709.

26. ArbeitskreisBlut, Untergruppe «BewertungBlutassoziierterKrankheitserreger». Influenza Virus. Transfus Med Hemother. 2009;36(1):32-39. doi: 10.1159/000197314. PMID: 21048819; PMCID: PMC2928832.

27. Lembo D, Donalisio M, Civra A, Argenziano M, Cavalli R. Nanomedicine formulations for the delivery of antiviral drugs: a promising solution for the treatment of viral infections. Expert Opin Drug Deliv. 2018 Jan; 15(1):93-114. doi: 10.1080/17425247.2017.1360863. Epub 2017 Aug 3. PMID: 28749739.

28. Cao Q, Wu H, Zhu L, Wu D, Zhu Y, Zhu Z, Cui J. Preparation and evaluation of zanamivir-loaded solid lipid nanoparticles. J Control Release. 2011 Nov 30; 152 Suppl1:e2-4. doi: 10.1016/j.jconrel.2011.08.085. PMID: 22195851.

29. Crimi S, Fiorillo L, Bianchi A, D'Amico C, Amoroso G, Gorassini F, Mastroieni R, Marino S, Scoglio C, Catalano F, Campagna P, Bocchieri S, De Stefano R, Fiorillo MT, Cicciù M. Herpes Virus, Oral Clinical Signs and QoL: Systematic Review of Recent Data. Viruses. 2019 May 21; 11(5):463. doi: 10.3390/v11050463. PMID: 31117264; PMCID: PMC6563194.

30. Perret F, Duffour M, Chevalier Y, Parrot-Lopez H. Design, synthesis, and in vitro evaluation of new amphiphilic cyclodextrin-based nanoparticles for the incorporation and controlled release of acyclovir. Eur J Pharm Biopharm. 2013 Jan; 83(1):25-32. doi: 10.1016/j.ejpb.2012.09.013. Epub 2012 Oct 13. PMID: 23072941.

31. Lembo D, Swaminathan S, Donalisio M, Civra A, Pastero L, Aquilano D, Vavia P, Trotta F, Cavalli R. Encapsulation of Acyclovir in new carboxylated cyclodextrin-based nanosponges improves the agent's antiviral efficacy. Int J Pharm. 2013 Feb 25; 443(1-2):262-72. doi: 10.1016/j.ijpharm.2012.12.031. Epub 2012 Dec 30. PMID: 23279938.

32. Morozov VA, Lagaye S. Hepatitis C virus: Morphogenesis, infection and therapy. World J Hepatol. 2018 Feb 27;1 0(2):186-212. doi: 10.4254/wjh.v10.i2.186. PMID: 29527256; PMCID: PMC5838439.

33. Alter MJ. Prevention of spread of hepatitis C. Hepatology. 2002 Nov; 36(5 Suppl 1):S93-8. doi: 10.1053/jhep.2002.36389. PMID: 12407581.

34. Lai L, Hui CK, Leung N, Lau GK. Pegylated interferon alpha-2a (40 kDa) in the treatment of chronic hepatitis B. Int J Nanomedicine. 2006; 1(3):255-62. PMID: 17717966; PMCID: PMC2426802.

35. De Clercq E, Férir G, Kaptein S, Neyts J. Antiviral treatment of chronic hepatitis B virus (HBV) infections. Viruses. 2010 Jun; 2(6):1279-305. doi: 10.3390/v2061279. Epub 2010 May 31. PMID: 21994680; PMCID: PMC3185710.

36. De Clercq E, Li G. Approved Antiviral Drugs over the Past 50 Years. Clin Microbiol Rev. 2016 Jul; 29(3):695-747. doi: 10.1128/CMR.00102-15. PMID: 27281742; PMCID: PMC4978613.

37. McKimm-Breschkin JL. Influenza neuraminidase inhibitors: antiviral action and mechanisms of resistance. Influenza Other Respir Viruses. 2013 Jan; 7 Suppl 1(Suppl 1):25-36. doi: 10.1111/irv.12047. PMID: 23279894; PMCID: PMC4942987.

38. Modi S, Van L, Gewirtzman A, Mendoza N, Bartlett B, Tremaine AM, Tyring S. Single-day treatment for orolabial and genital herpes: a brief review of pathogenesis and pharmacology. Ther Clin Risk Manag. 2008 Apr; 4(2):409-17. doi: 10.2147/tcrm.s1664. PMID: 18728852; PMCID: PMC2504076.

39. De Clercq E, Li G. Approved Antiviral Drugs over the Past 50 Years. Clin Microbiol Rev. 2016 Jul; 29(3):695-747. doi: 10.1128/CMR.00102-15. PMID: 27281742; PMCID: PMC4978613.

40. Sharp PM, Hahn BH. Origins of HIV and the AIDS pandemic. Cold Spring HarbPerspect Med. 2011 Sep; 1(1):a006841. doi: 10.1101/cshperspect.a006841. PMID: 22229120; PMCID: PMC3234451.

41. Arts Eric J,Daria HJ.Hiv -1 Antiretroviral drug therapy . Cold Spring HarbPerspect Med. 2012; 2(4):a007161.

42. McGowan I. An overview of antiretroviral pre-exposure prophylaxis of HIV infection. Am J Reprod Immunol. 2014 Jun; 71(6):624-30. doi: 10.1111/aji.12225. Epub 2014 Mar 17. PMID: 24635047.

43. Usach I, Melis V, Peris JE. Non-nucleoside reverse transcriptase inhibitors: a review on pharmacokinetics, pharmacodynamics, safety and tolerability. J Int AIDS Soc. 2013 Sep 4; 16(1):1-14. doi: 10.7448/IAS.16.1.18567. PMID: 24008177; PMCID: PMC3764307.

44. Liao C, Marchand C, Burke TR Jr, Pommier Y, Nicklaus MC. Authentic HIV-1 integrase inhibitors. Future Med Chem. 2010 Jul; 2(7):1107-22. doi: 10.4155/fmc.10.199. PMID: 21426159; PMCID: PMC3413320.

45. Lv Z, Chu Y, Wang Y. HIV protease inhibitors: a review of molecular selectivity and toxicity. HIV AIDS (Auckl). 2015 Apr 8; 7:95-104. doi: 10.2147/HIV.S79956. PMID: 25897264; PMCID: PMC4396582.

46. Qian K, Morris-Natschke SL, Lee KH. HIV entry inhibitors and their potential in HIV therapy. Med Res Rev. 2009 Mar; 29(2):369-93. doi: 10.1002/med.20138. PMID: 18720513; PMCID: PMC3773846.

47. De Clercq E, Li G. Approved Antiviral Drugs over the Past 50 Years. Clin Microbiol Rev. 2016 Jul; 29(3):695-747. doi: 10.1128/CMR.00102-15. PMID: 27281742; PMCID: PMC4978613.

48. Singh L, Kruger HG, Maguire GEM, Govender T, Parboosing R. The role of nanotechnology in the treatment of viral infections. Ther Adv Infect Dis. 2017 Jul; 4(4):105-131. doi: 10.1177/2049936117713593. Epub 2017 Jul 5. PMID: 28748089; PMCID: PMC5507392.

49. Schütz CA, Juillerat-Jeanneret L, Mueller H, Lynch I, Riediker M; NanoImpactNet Consortium. Therapeutic nanoparticles in clinics and under clinical evaluation. Nanomedicine (Lond). 2013 Mar; 8(3):449-67. doi: 10.2217/nnm.13.8. PMID: 23477336.

50. Mehendale R, Joshi M, Patravale VB. Nanomedicines for treatment of viral diseases. Crit Rev Ther Drug Carrier Syst. 2013; 30(1):1-49. doi: 10.1615/critrevtherdrugcarriersyst.2013005469. PMID: 23510109.

51. Parboosing R, Maguire GE, Govender P, Kruger HG. Nanotechnology and the treatment of HIV infection. Viruses. 2012 Apr; 4(4):488-520. doi: 10.3390/v4040488. Epub 2012 Apr 10. PMID: 22590683; PMCID: PMC3347320.

52. Wong HL, Chattopadhyay N, Wu XY, Bendayan R. Nanotechnology applications for improved delivery of antiretroviral drugs to the brain. Adv Drug Deliv Rev. 2010 Mar 18; 62(4-5):503-17. doi: 10.1016/j.addr.2009.11.020. Epub 2009 Nov 13. PMID: 19914319.

53. Lembo D, Cavalli R. Nanoparticulate delivery systems for antiviral drugs. Antivir Chem Chemother. 2010; 21(2):53-70. doi: 10.3851/IMP1684. PMID: 21107015.

54. Mehendale R, Joshi M, Patravale VB. Nanomedicines for treatment of viral diseases. Crit Rev Ther Drug Carrier Syst. 2013; 30(1):1-49. doi: 10.1615/critrevtherdrugcarriersyst.2013005469. PMID: 23510109.

55. Mahapatro A, Singh DK. Biodegradable nanoparticles are excellent vehicle for site directed in-vivo delivery of drugs and vaccines. J Nanobiotechnology. 2011 Nov 28; 9:55. doi: 10.1186/1477-3155-9-55. PMID: 22123084; PMCID: PMC3238292.

56. Chattopadhyay N, Zastre J, Wong HL, Wu XY, Bendayan R. Solid lipid nanoparticles enhance the delivery of the HIV protease inhibitor, atazanavir, by a human brain endothelial cell line. Pharm Res. 2008 Oct; 25(10):2262-71. doi: 10.1007/s11095-008-9615-2. Epub 2008 May 31. PMID: 18516666.

57. GongP, LiH, He X, Wang K, Hu J, Tan W, ZhangS, YangX. Preparation and antibacterial activity of Fe304 Ag NP. Nanotechnology. 2007 Nov 28. 18:285-604.

58. Elechiguerra JL, Burt JL, Morones JR, Camacho-Bragado A, Gao X, Lara HH, Yacaman MJ. Interaction of silver nanoparticles with HIV-1. J Nanobiotechnology. 2005 Jun 29; 3:6. doi: 10.1186/1477-3155-3-6. PMID: 15987516; PMCID: PMC1190212.

59. Cui Y, Zhao Y, Tian Y, Zhang W, Lü X, Jiang X. The molecular mechanism of action of bactericidal gold nanoparticles on Escherichia coli. Biomaterials. 2012 Mar; 33(7):2327-33. doi: 10.1016/j.biomaterials.2011.11.057. Epub 2011 Dec 17. PMID: 22182745.

60. Rafiei S, Rezatofighi SE, RoayaeiArdakani M, Rastegarzadeh S. Gold Nanoparticles Impair Foot-and-Mouth Disease Virus Replication. IEEE Trans Nanobioscience. 2016 Jan; 15(1):34-40. doi: 10.1109/TNB.2015.2508718. Epub 2015 Dec 17. PMID: 26685261.

61. Ahmed SR, Kim J, Suzuki T, Lee J, Park EY. Detection of influenza virus using peroxidase-mimic of gold nanoparticles. BiotechnolBioeng. 2016 Oct; 113(10):2298-303. doi: 10.1002/bit.25982. Epub 2016 Aug 9. PMID: 27002303.

62. Soares S, Sousa J, Pais A, Vitorino C. Nanomedicine: Principles, Properties, and Regulatory Issues. Front Chem. 2018 Aug 20; 6:360. doi: 10.3389/fchem.2018.00360. PMID: 30177965; PMCID: PMC6109690.

63. Tyssen D, Henderson SA, Johnson A, Sterjovski J, Moore K, La J, Zanin M, Sonza S, Karellas P, Giannis MP, Krippner G, Wesselingh S, McCarthy T, Gorry PR, Ramsland PA, Cone R, Paull JR, Lewis GR, Tachedjian G. Structure activity relationship of dendrimer microbicides with dual action antiviral activity. PLoS One. 2010 Aug 23; 5(8):e12309. doi: 10.1371/journal.pone.0012309. PMID: 20808791; PMCID: PMC2925893.

64. Pradhan D, Biswasroy P, Goyal A, Ghosh G, Rath G. Recent Advancement in Nanotechnology-Based Drug Delivery System Against Viral Infections. AAPS PharmSciTech. 2021 Jan 14; 22(1):47. doi: 10.1208/s12249-020-01908-5. PMID: 33447909; PMCID: PMC7808403.

65. Lembo D, Cavalli R. Nanoparticulate delivery systems for antiviral drugs. Antivir Chem Chemother. 2010; 21(2):53-70. doi: 10.3851/IMP1684. PMID: 21107015.

66. Letchford K, Burt H. A review of the formation and classification of amphiphilic block copolymer nanoparticulate structures: micelles, nanospheres, nanocapsules and polymersomes. Eur J Pharm Biopharm. 2007 Mar; 65(3):259-69. doi: 10.1016/j.ejpb.2006.11.009. Epub 2006 Nov 23. PMID: 17196803.

67. Milovanovic M, Arsenijevic A, Milovanovic J, Kanjevac T, Arsenijevic N. Nanoparticles in Antiviral Therapy. Antimicrobial Nanoarchitectonics. 2017; 383–410. doi: 10.1016/B978-0-323-52733-0.00014-8. Epub 2017 Jun 30. PMCID: PMC7173505.

68. Moretton MA, Glisoni RJ, Chiappetta DA, Sosnik A. Molecular implications in the nanoencapsulation of the anti-tuberculosis drug rifampicin within flower-like polymeric micelles. Colloids Surf B Biointerfaces. 2010 Sep 1; 79(2):467-79. doi: 10.1016/j.colsurfb.2010.05.016. PMID: 20627665.

69. Jaiswal M, Dudhe R, Sharma PK. Nanoemulsion: an advanced mode of drug delivery system. 3 Biotech. 2015 Apr; 5(2):123-127. doi: 10.1007/s13205-014-0214-0. Epub 2014 Apr 8. PMID: 28324579; PMCID: PMC4362737.

70. Furin JJ, Behforouz HL, Shin SS, Mukherjee JS, Bayona J, Farmer PE, Kim JY, Keshavjee S. Expanding global HIV treatment: case studies from the field. Ann N Y Acad Sci. 2008; 1136:12-20. doi: 10.1196/annals.1425.004. Epub 2007 Oct 22. PMID: 17954668.

71. Chiodo F, Marradi M, Calvo J, Yuste E, Penadés S. Glycosystems in nanotechnology: Gold glyconanoparticles as carrier for anti-HIV prodrugs. Beilstein J Org Chem. 2014 Jun 12; 10:1339-46. doi: 10.3762/bjoc.10.136. PMID: 24991287; PMCID: PMC4077455.

72. Destache CJ, Belgum T, Goede M, Shibata A, Belshan MA. Antiretroviral release from poly(DL-lactide-co-glycolide) nanoparticles in mice. J Antimicrob Chemother. 2010 Oct; 65(10):2183-7. doi: 10.1093/jac/dkq318. Epub 2010 Aug 21. PMID: 20729545; PMCID: PMC2941676.

73. Jenita JL, Chocalingam V, Wilson B. Albumin nanoparticles coated with polysorbate 80 as a novel drug carrier for the delivery of antiretroviral drug-Efavirenz. Int J Pharm Investig. 2014 Jul; 4(3):142-8. doi: 10.4103/2230-973X.138348. PMID: 25126528; PMCID: PMC4131386.

74. Katas H, Alpar HO. Development and characterisation of chitosan nanoparticles for siRNA delivery. J Control Release. 2006 Oct 10; 115(2):216-25. doi: 10.1016/j.jconrel.2006.07.021. Epub 2006 Jul 25. PMID: 16959358.

75. Elberry MH, Darwish NHE, Mousa SA. Hepatitis C virus management: potential impact of nanotechnology. Virol J. 2017

May 2; 14(1):88. doi: 10.1186/s12985-017-0753-1. PMID: 28464951; PMCID: PMC5414367.

76. Liu G, Xu D, Jiang M, Yuan W. Preparation of bioactive interferon alpha-loaded polysaccharide nanoparticles using a new approach of temperature-induced water phase/water-phase emulsion. Int J Nanomedicine. 2012; 7:4841-8. doi: 10.2147/IJN.S35502. Epub 2012 Sep 7. Retraction in: Int J Nanomedicine. 2018 Apr 19; 13:2277. PMID: 22973103; PMCID: PMC3439862.

77. Jiménez-Pardo I, González-Pastor R, Lancelot A, Claveria-Gimeno R, Velázquez-Campoy A, Abian O, Ros MB, Sierra T. Shell Cross-Linked Polymeric Micelles as Camptothecin Nanocarriers for Anti-HCV Therapy. MacromolBiosci. 2015 Oct; 15(10):1381-91. doi: 10.1002/mabi.201500094. Epub 2015 Jun 5. PMID: 26045353.

78. Lee MY, Yang JA, Jung HS, Beack S, Choi JE, Hur W, Koo H, Kim K, Yoon SK, Hahn SK. Hyaluronic acid-gold nanoparticle/interferon α complex for targeted treatment of hepatitis C virus infection. ACS Nano. 2012 Nov 27; 6(11):9522-31. doi: 10.1021/nn302538y. Epub 2012 Oct 26. PMID: 23092111.

79. Nanda A, Saravanan M. Biosynthesis of silver nanoparticles from Staphylococcus aureus and its antimicrobial activity against MRSA and MRSE. Nanomedicine. 2009 Dec; 5(4):452-6. doi: 10.1016/j.nano.2009.01.012. Epub 2009 Feb 13. PMID: 19523420.

80. Ishihara T, Kaneko K, Ishihara T, Mizushima T. Development of biodegradable nanoparticles for liver-specific ribavirin delivery. J Pharm Sci. 2014 Dec; 103(12):4005-4011. doi: 10.1002/jps.24219. Epub 2014 Oct 21. PMID: 25335768.

81. Abo-Zeid YM, Urbanowicz RA, Tarr AW, Irving WL, Thomson BJ, Garnett MC. Nanoparticles as a promising delivery system to improve hepatitis C treatment (2014). www.semanticscholar.org/paper/Nanoparticles-as-a-Promising-Delivery-System-to-C-Abo-zeid-Urbanowicz/653ba60c026716b8f040cefa70f86ceedfb037b4

82. Ryoo SR, Jang H, Kim KS, Lee B, Kim KB, Kim YK, Yeo WS, Lee Y, Kim DE, Min DH. Functional delivery of DNAzyme with iron oxide nanoparticles for hepatitis C virus gene knockdown. Biomaterials. 2012 Mar; 33(9):2754-61. doi: 10.1016/j.biomaterials.2011.12.015. Epub 2011 Dec 27. PMID: 22206595.

83. Ge Q, Dallas A, Ilves H, Shorenstein J, Behlke MA, Johnston BH. Effects of chemical modification on the potency, serum stability, and immunostimulatory properties of short shRNAs. RNA. 2010 Jan; 16(1):118-30. doi: 10.1261/rna.1901810. Epub 2009 Nov 30. PMID: 19948766; PMCID: PMC2802022.

84. Al-Dhubiab BE, Nair AB, Kumria R, Attimarad M, Harsha S. Formulation and evaluation of nano based drug delivery system for the buccal delivery of acyclovir. Colloids Surf B Biointerfaces. 2015 Dec 1; 136:878-84. doi: 10.1016/j.colsurfb.2015.10.045. Epub 2015 Oct 31. PMID: 26547315.

85. Baram-Pinto D, Shukla S, Perkas N, Gedanken A, Sarid R. Inhibition of herpes simplex virus type 1 infection by silver nanoparticles capped with mercaptoethane sulfonate. Bioconjug Chem. 2009 Aug 19; 20(8):1497-502. doi: 10.1021/bc900215b. Epub 2009 Jul 8. PMID: 21141805.

86. Szymańska E, Orłowski P, Winnicka K, Tomaszewska E, Bąska P, Celichowski G, Grobelny J, Basa A, Krzyżowska M. Multifunctional Tannic Acid/Silver Nanoparticle-Based Mucoadhesive Hydrogel for Improved Local Treatment of HSV Infection: In Vitro and In Vivo Studies. Int J Mol Sci. 2018 Jan 28; 19(2):387. doi: 10.3390/ijms19020387. PMID: 29382085; PMCID: PMC5855609.

87. Seyfoddin A, Al-Kassas R. Development of solid lipid nanoparticles and nanostructured lipid carriers for improving ocular delivery of acyclovir. Drug Dev Ind Pharm. 2013 Apr; 39(4):508-19. doi: 10.3109/03639045.2012.665460. Epub 2012 Mar 19. PMID: 22424312.

88. Xiang DX, Chen Q, Pang L, Zheng CL. Inhibitory effects of silver nanoparticles on H1N1 influenza A virus in vitro. J Virol Methods. 2011 Dec; 178(1-2):137-42. doi: 10.1016/j.jviromet.2011.09.003. Epub 2011 Sep 17. PMID: 21945220.

89. MazurkovaaNA, SpitsynaaYE, ShikinacN.V, IsmagilovcZR, Zagrebel'nyia SN,Ryabchikovaa EI.Interaction of titanium dioxide nanoparticle with influenza virus.Nanotechnology Russia. 2010; 5:417-420.

90. Tao W, Ziemer KS, Gill HS. Gold nanoparticle-M2e conjugate coformulated with CpG induces protective immunity against influenza A virus. Nanomedicine (Lond). 2014 Feb; 9(2):237-51. doi: 10.2217/nnm.13.58. Epub 2013 Jul 5. PMID: 23829488; PMCID: PMC3958969.

91. Papp I, Sieben C, Ludwig K, Roskamp M, Böttcher C, Schlecht S, Herrmann A, Haag R. Inhibition of influenza virus infection by multivalent sialic-acid-functionalized gold nanoparticles. Small. 2010 Dec 20; 6(24):2900-6. doi: 10.1002/smll.201001349. PMID: 21104827.

92. Ghaffari H, Tavakoli A, Moradi A, Tabarraei A, Bokharaei-Salim F, Zahmatkeshan M, Farahmand M, Javanmard D, Kiani SJ, Esghaei M, Pirhajati-Mahabadi V, Monavari SH, Ataei-Pirkooh A. Inhibition of H1N1 influenza virus infection by zinc oxide nanoparticles: another emerging application of nanomedicine. J Biomed Sci. 2019 Sep 10; 26(1):70. doi: 10.1186/s12929-019-0563-4. PMID: 31500628; PMCID: PMC6734352.

93. Sharma D, Ali AAE, Trivedi LR; An Updated Review on: Liposomes as drug delivery system; PharmaTutor; 2018; 6(2):50-62; http://dx.doi.org/10.29161/PT.v6.i2.2018.50

94. Sharma, D., & Kosankar, K. V. Green Tea in Green World an updated review. PharmaTutor, 2018; 6(3):9-16. https://doi.org/10.29161/PT.v6.i3.2018.9.

95. Shweta Parihar, Devender Sharma, "NAVAGRAHA(NINE PLANETS) PLANTS: THE TRADITIONAL USES AND THE THERAPEUTIC POTENTIAL OF NINE SACRED PLANTS OF INDIA THAT SYMBOLISES NINE PLANETS", International Journal of Research and Analytical Reviews (IJRAR), 2021; 8(4):96-108.

96. Sharma, D., & Bhujbale, A. A. Phytosomes is a Novel Drug Delivery System based herbal formulation: An Review. PharmaTutor, 2018; 6(3):23-26. https://doi.org/10.29161/PT.v6.i3.2018.23

97. Sharma, D. Microneedles: an approach in transdermal drug delivery: a Review. PharmaTutor, 2018; 6(1):7-15. https://doi.org/10.29161/PT.v6.i1.2018.7.

98. Sharma, D., Ali, A. A. E., & Aate, J. R. Niosomes as Novel Drug Delivery System: Review Article. PharmaTutor, 2018; 6(3):58-65. https://doi.org/10.29161/PT.v6.i3.2018.58

99. Chaudhary, K., & Sharma, D. Cubosomes: A Potential Drug Delivery System. Asian Journal of Pharmaceutical Research and Development, 2021; 9(5):93-101. https://doi.org/https://doi.org/10.22270/ajprd.v9i5.981.

100. Lanjewar, A., Maurya, S., Sharma, D., & Gaur, A. Review on Hair Problem and its Solution. Journal of Drug Delivery and Therapeutics, 2020; 10(3-s):322-329. https://doi.org/10.22270/jddt.v10i3-s.4066