Chapter 27

Nanoparticle-Mediated Antimicrobial Armory: Employing Nanotechnology for Precision Control of Bacterial and Viral Infections

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ABSTRACT

This chapter gives us details about the complex role of nanoparticles in dealing with bacteria and viruses as antimicrobial agents. Nanoparticles are tiny particles with a size of 1- 100 nm. Their properties are very unique so a lot of research is carried out on these revolutionary particles. They are present in nature and have a very ancient history. The evolution of these particles from ancient history to Michael Faraday's work is tracked which can elaborate their importance in modern medicine and industry fields. The classification of these particles into various types such as organic and inorganic nanoparticles helps us to study their antimicrobial activity in detail. Further, this chapter explores the antibacterial properties of nanoparticles. Organic nanoparticles such as liposomes and inorganic nanoparticles such as gold and silver nanoparticles destroy the cell walls of bacteria by different mechanisms of action. The importance of nanoparticles increases more because they can be an alternative to antibiotics in case of AMR which is a big threat to the world nowadays. This chapter also delves into the antiviral properties of nanoparticles. Viral infections are a big threat to society and unfortunately, they have no specific treatments but nanoparticles can be used to prepare vaccination that can be used against these viruses with more precise targeting mechanisms.

KEYWORDS		
Bacteria, Viruses, Chemical drugs, Resistance, Alternative, Nanoparticles	Received: 18-Jun-2024 Revised: 14-Jul-2024 Accepted: 16-Aug-2024	A Publication of Unique Scientific Publishers

Cite this Article as: Javed MU, Fatima T, Amir MH, Naveed MT, Liaqat N, Abdullah M, Amin MA, Rehman TU, Yousaf F and Javed MZH, 2024. Nanoparticle-mediated antimicrobial armory: employing nanotechnology for precision control of bacterial and viral infections. In: Ahmed R, Khan A, Abbas RZ, Farooqi SH and Asrar R (eds), Complementary and Alternative Medicine: Nanotechnology-II. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 233-242. https://doi.org/10.47278/book.CAM/2024.309

INTRODUCTION

Nanoparticles are matter particles (Griffin et al., 2017), have a small size of 1-100 nanometers (Paulami et al., 2023; Tripathi et al., 2023), and can't be seen with the naked human eye or even with the compound microscope. (Diaspro et al., 2022; M. Ismail et al., 2019) The electron microscope is required to see nanoparticles (Dahy et al., 2023). They are also called ultrafine particles (Li et al., 2016; Burtscher et al., 2012). Nanoparticles are widely present in nature (Suhag et al., 2023; Niu et al., 2023). They play an important role in modern medicines (Joseph et al., 2023; Munir et al., 2020) and are present in many industrial products (Litter et al., 2023; Malik et al., 2023) like plastic (Majeed et al., 2024, Calovi et al. 2023), paints, metallic (Santos et al., 2015) and magnetic products (Zerkani and Abbodi, 2023). Their roles are very deeply studied in different sciences such as chemistry, physics, and even in medical science to treat different diseases (Zahin et al. 2020).

They are generated through a lot of naturally occurring events in the Universe (Buzea et al., 2007) e.g. volcanic eruptions (Ermulin et al., 2023; Fedotov et al., 2023), microbial processes (Milani et al., 2023), forest fires (Nim et al., 2023), etc. There is a very unique history of Nanoparticles. Artists have used nanoparticles in their crafts but they didn't know their properties since prehistory (Montanarella and Kovalenko, 2022). Many artifacts of ancient times showed that tiny metal particles were mixed with different materials to make them unique. The example of the Lycurgus Cup is perfect in which nanoparticles were used for their color-changing characteristics but at that time artists didn't know about it (Babu et al., 2023; Khatun and Predeep, 2023). The unique visual was obtained by mixing silver and gold nanoparticles in glass which interact with light and give beautiful visions (Litter and Ahmad, 2023). Similarly, Mesopotamia lusterware pottery shows a beautiful metallic shine due to metallic nanoparticles of copper and silver in the glass. (Jayalatha and Rayappan, 2015; Mirguet et al., 2015). The ancient artist manipulated things at the nano level, making remarkable achievements in their creations. (Heiligtag and Niederberger, 2013). In the 19th century, Michael Faraday gave scientific knowledge of nanoparticle-scale metal properties in his paper in 1857 (Merupa et al., 2023; Norton et al., 2023). He observed that heating mounted gold or silver thin leaves on the glass below red heat changes their properties, it changes light transmission and reflection in these metals and their electricity resistivity also increases (Stempski et al., 2019; Parveen et al., 2016). The interaction of light with nanoparticles was described by Mie in 1908 (Dorodnayy et al., 2023; Talapin and Shevchenko, 2016).

In the 1970s and 80s, proper studies started in America and Japan (Litter and Ahmad, 2023; Ma, 2022). In the beginning, they called them ultrafine particles, but by the 1990s the term nanoparticle became more common. The National Nanotechnology Initiative started in America officially in 2000 (Roco, 2023; Hashmin et al., 2022).

Nanoparticles are very useful in all science subjects but our topic is related to the use of nanoparticles in antimicrobial resistance and control. Nanoparticles are classified into different types based on physiochemical compositions (Khan, 2019; Stone et al., 2010) e.g. Organic based nanoparticles (nanocapsule, nanosphere, liposomes, dendrimers), Inorganic based nanoparticles (silver, gold, magnetic and alloy nanoparticles.), carbon-based Nps, semiconductor-based nanoparticles, etc.

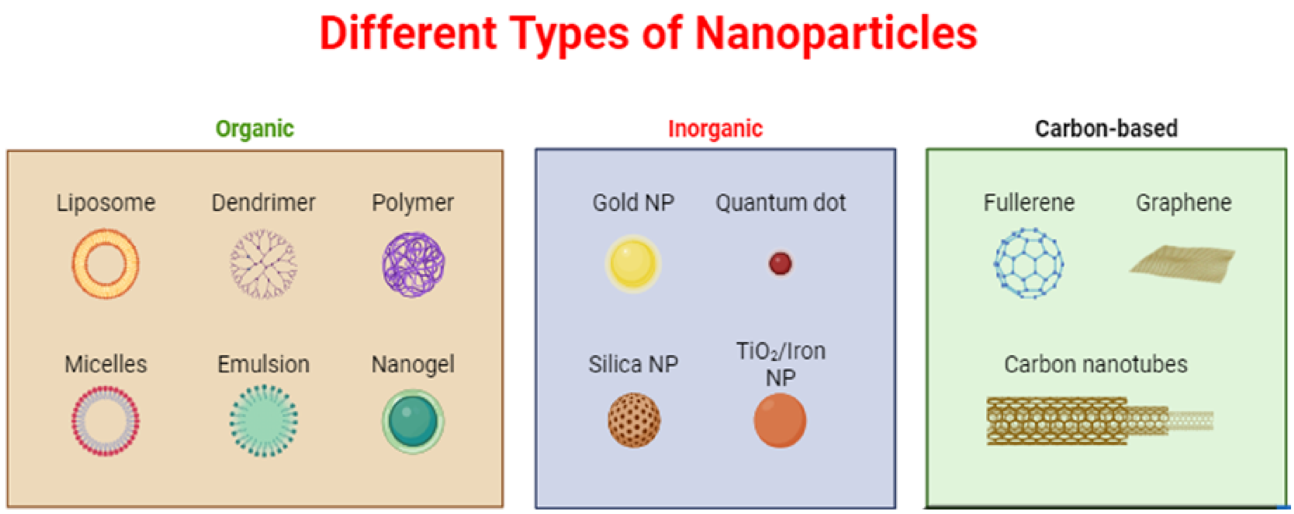
Organic Nanoparticle is the type of nanoparticle used in drug delivery systems (Natesan and Kim, 2023; Ulises and Sharma, 2023; Mitragotri et al., 2014). Following are some organic nanoparticles. Nanocapsule are hollow spheres (Vasilaki et al., 2023; Panigrahi et al., 2022) in which the drug is confined in the inner cavity with a polymer coating (Anis et al. 2023; Li et al., 2023) their size is 50-300 nm (Verma et al., 2016). They have low density but higher loading capacity (Wu et al., 2020; Geothals et al., 2013). Nanospheres are a matrix system of drug delivery in which the drug is spread uniformly (Purabisaha et al., 2021). Their size ranges from 100-200 nm (Barcelo et al., 2012). In many studies, they are used to treat influenza (Cho et al., 2015), Hepatitis B (Wen et al., 2019), and Herpes Simplex Virus (Shen et al., 2019).

Liposomes (Li et al., 2023) are a type of Organic NP that is very important. They are spherical carriers with tiny sizes of 20-30 nm (Nsairat et al., 2022). They are made up of a phospholipid bilayer that surrounds the aqueous core (Rai et al., 2014). Phospholipid bilayer gives them a very unique quality. They can mimic cell membranes and easily fuse with microbial cell membranes (Fang et al., 2015). Drugs can be mixed in the inner core for targeted drug delivery. They are non-toxic and biodegradable (Farid et al., 2020; Singh et al, 2017) Inorganic nanoparticles are smaller than organic nanoparticles but have More efficacy.

Silver nanoparticles are a Great role of nanoparticles these days in different fields but among all of the types, silver NP are a more widely used type. They are used in large quantities in the industry to make home appliances, water treatment plants, and disinfectants used in the medical field (Saifuddin et al., 2017). They are also used in biosensing and imaging technology due to their unique properties (Garg et al., 2020; Siromani and Daniel, 2011). AG NP is also very effective in treating many diseases by targeting specific cells (Franci et al., 2015) e.g. Ag NP targets the HIV-1 virus by stopping it from binding with host cells in vitro (Alarcon and Udekwu, 2015; Tsai et al., 2019)

Gold nanoparticles are synthesized in large quantities because they are used in many medical treatments e.g. treatment of PPR in ruminants (Bisht et al., 2023). They have a very important role in the medication of different infections. They are made from Tetra chloroauric acid (HAuCl4) and Trisodium citrate by a reduction process in an aqueous solution (Hammami et al., 2021). Their surface plasmon resonance properties make them suitable for imaging techniques and biomedical tools (Verma and Singh, 2014). They are used to detect DNA in a sample as a lab tracer. They can be used to detect aminoglycoside antibiotics. They are used to detect cancer stem cells which are very useful in cancer diagnosis (Hasan, 2015).

Magnetic nanoparticles are also a very important type. They are made up of metallic elements like iron, cobalt, and nickel and their oxides under an external magnetic field (Selim et al., 2023). They are used in MRI and targeted drug and gene delivery (Shen et al., 2018; Shubayev et al, 2009).



Nanoparticle: Tiny Warriors against Microbes

Nanoparticles are the modern and ting fighters that fight against microbes (Mobeen et al., 2021). They can solve many problems caused by bacterial and viral infections (Baptista et al., 2018). They can target the pathogens very accurately and kill them in different ways even if they develop resistance to antibiotics (Natan and Banin, 2017). This seems very fictional but it's reality now.

In present days, bacterial infections are treated with antibiotics which is a very useful way to overcome infections which is very good but we need these futuristic technologies. The reason behind this is microbial resistance against these antibiotics. Microbial resistance is a big threat these days (Muteeb et al., 2023; Tang et al., 2023). Many antibiotics are not useful for many bacterial infections nowadays because bacteria develop resistance against these antibiotics and they aren't able to kill these bacteria anymore (Costanzo and Roviello, 2023). Superbugs and multidrug-resistant bacteria are endemic in many parts of the world (Aslam et al., 2023; Panuli et al., 2023). This is the start of resistance as time proceeds all bacteria may develop resistance and infections become untreatable. Before this happens, we have to develop alternatives to these antibiotics. (Christaki, Marcou, and Tofarides, 2020)

Nanoparticles can easily alternate these conventional antibiotics (Kanwar et al., 2023). They can not only work against bacterial infection but also against viral infections, which is the best thing about them (Teirumnieks et al., 2023; Aguilera et al., 2021). Nanoparticles have a high surface area-to-volume ratio, tailored surface properties, and customizable composition (Schneider et al., 2021). These properties make nanoparticles act against the pathogen. Nanoparticles can also be designed to specifically target microbial cells while minimizing adverse effects on host cells (Sethu et al. 2017). They are also concerned with toxicity, scalability, and regulatory factors.

They can be used in wound dressing (Kalantari et al., 2020), coating for medical devices (Marassi et al. 2018), and as delivery systems for antimicrobial drugs (Canaparo et al., 2019). Nanoparticles play a role in water purification systems by effectively eliminating bacteria eliminating bacterial contaminants (Joseph et al., 2023). Future research aims to optimize nanoparticles for improved efficacy, biocompatibility, and scalability.

Nanoparticles as Precision Tools against Bacterial Infection

Nanoparticles have emerged as strong candidates for fighting against bacterial infections with unique properties and applications (Khan and Rasool, 2023). By functionalizing the surface of nanoparticles, scientists can design them to recognize and bind selectively to bacterial cell surfaces (Ho et al. 2004). This gives a specific targeting approach to nanoparticles. Nanoparticles have a different way of interacting with bacteria. Some penetrate bacterial cell walls (Mei et al., 2013), destroy cell wall integrity, and cause cell death. Some release antimicrobial compounds or generate reactive oxygen species which stop bacterial growth and interact with important cellular processes, making them effective antibacterial agents (Karanwal et al. 2023).

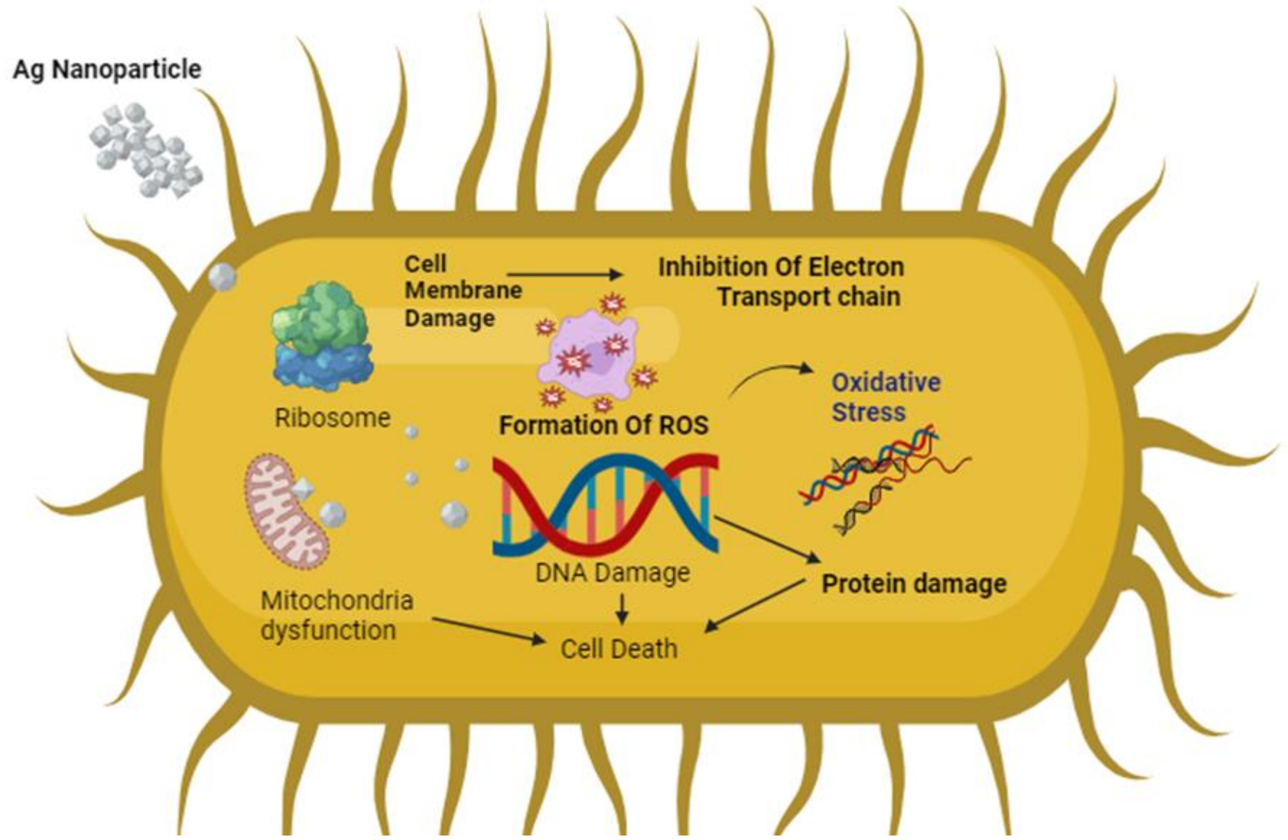
The rise of antibiotic-resistant bacteria can be treated with nanoparticle solutions. Nanoparticles can fight against resistance strains through multiple MOA making them effective against multidrug-resistant bacteria. (Cui and Zhang, 2012). In bacterial infection, vascular permeability increases due to the release of bacterial components which trigger an inflammatory response and malfunction in the body's defense system. Nanoparticles take advantage of it and enhance permeation and retention for targeted antibiotic delivery to the site of infection (Gao et al., 2014). Bacteria usually maintain a negative surface charge, nanoparticles that are positively charged are designed to bind to bacteria through electrostatic interaction and neutralize the bacteria (Tan and Onur, 2018; Wang and Shao, 2017).

Nanoparticles can be functionalized with a pathogen-binding ligand such as small molecules e.g. lectins, antibiotics, or bacteriophage proteins. These ligands help in specific binding to bacteria which increases the precision of nanoparticles to target specific pathogens (Yeh et al., 2020). Macrophages can take the nanoparticle to the targeted site through passive or ligand-mediated mechanisms which improves antibiotic therapy, particularly for intracellular bacterial infections (Gao et al., 2014). Some nanoparticle-based vaccines are also made which can treat and produce immunity against bacterial infections (Lin et al., 2018).

Nanoparticles provide us with a solution to problems faced by traditional vaccines. By conjugating antigen to the nanoparticle surface, b-cell activation is facilitated due to increased antigen delivery to antigen-presenting cells. modern fabrication methods like layer-by-layer and cellular membrane-coated nanoparticles increase antigen loading and immune modulation (Bezbaruah et al., 2022). Nanoparticles allow for the parallel delivery of antigens and adjuvants that mimic natural microbes (Gao et al., 2014). Toll-like receptor ligands can be delivered using nanoparticles that boost the immune response (Haegebaert et al., 2022).

Nanoparticles can be delivered very specifically at specific sites safely and effectively. For example, pH-responsive nanoparticles protect antigens in the stomach and release them in lower GIT for translocation across in intestinal epithelium (Gao and Zhang, 2014). Nanoparticles are also used in the detection of bacterial infections in different parts of the body (Aflakian et al., 2023). Silica nanoparticles which have various fluorescent molecules enable ultrasensitive bacterial infection at single cell level (Gao et al., 2014). Semiconductor dots are used for sensitive bacterial detection and help in identifying different strains of bacteria (Zhang et al., 2023). Iron oxide nanoparticles are used to isolate bacteria from blood samples (Al-Rawi et al., 2021). Microfluidic systems with these nanoparticles allow high-throughput bacterial detection (Zhou et al., 2019). Paramagnetic iron oxide nanoparticles help in the detection of ultra-sensitive bacteria by using an MRI system (Gao et al., 2014).

Gold nanoparticles have unique properties that help in the detection of bacterial infections aggregation of gold nanoparticles due to changes in the plasmon resonance spectrum is used to detect bacterial DNAs and proteins (Mehrabi et al, 2023).



Mechanism of Action:

Nanoparticles interact differentially with different organisms (Deng et al., 2017). The nanoparticles also have different modes of action. Some nanoparticles bind with the cell wall. Some are attached to the protein of the cell. Silver NPs damage the membrane (Duran et al., 2016), bind protein to inactive it (Banerjee and Das, 2013), and stop the replication of DNA (Abbas et al., 2019). In *E. coli*, Ag NPs accumulate the enveloped protein in the cytoplasm by disappearing the proton motive force (Rao et al., 2022). This accumulation stops the proper functioning of protein in the membrane. In Staphylococcus aureus, AG NPs elevate the formate acetyltransferase which forms an anaerobic condition and reduces recombinase A which is related to DNA repair in this species (Cui et al., 2012).

TiO2 and ZnO NPs kill bacteria by producing reactive oxygen species (hydroxyl radical and hydrogen peroxide) under exposure to UV radiation (Leung et al. 2016). Gold NPs have a very unique mode of action. They disorganize the cell membrane, attach to nucleic acid, and stop the production of protein (Cui et al., 2012). Thus, they kill bacteria. They have bactericidal properties against *E. coli* (Hameed et al. 2020; Cui et al., 2012). Gold NPs exert their antimicrobial action in two ways: one is to change the potential of the membrane and stop the production of ATP Synthase due to which synthesis of ATP stops and general metabolism decreases. The other is they stop the subunit of Ribosome from binding with tRNA. AU NPs also increase the chemotaxis in early-phase reactions (Cui and Zhang, 2012).

Nanotechnology's Role In Combating Viral Infections

Nanoparticles play an important role in fighting against viral infections (Rai et al., 2016). It helps in the detection, diagnosis, treatment, and prevention of viral infections (Yadavalli and Shukla et al., 2017). Nanoparticles can be used to detect viral infections. It helps in the development of highly sensitive and specific diagnostic tools for viral infections (Koudelka et al. 2015). Nanoparticle-based assays such as quantum dots and gold nanoparticles increase the sensitivity of PCR and immunoassay to detect viral infections easily (Banerjee et al., 2018).

Nanoparticles are an effective carrier for antiviral drugs to be delivered at targeted sites (Maus et al., 2021). Lipid-based nanoparticles, polymeric nanoparticles, and dendrimers enable controlled release and increased bioavailability of antiviral agents (Chakraverty and Vora, 2021). This targeted delivery can minimize the adverse effects of drugs and maximize the therapeutic effects against viral infections. Nanoparticles are also used in important vaccines against viral infection (Szulczewski et al., 2018). Nanoparticles are used to boost the immune system by mimicking viral agents (Li et al., 2021). Nanoparticle-based vaccines are more stable and have more efficacy against infections (Diaz-Arevalo et al., 2020). They promote immune responses and help in targeted approaches to immune cells.

Nanoparticle types	MOA	Average size	Bacterial strains	Reference
Au	Damage Cell membrane	20-30 nm	Drug-Resistant *S. aureus, k. pnueumoniae* and *E. coli*	Predeepa et al., 2016
Ag	Stop replication of DNA	12-15 nm	*S. aureus, E. coli, S. typhimurium*	Bajaj et al., 2017
Fe3O4-Ag	Increased hydrophilicity	20-25 nm	*S. aureus, E. coli*	Zomorodian et al., 2018
MnFe2O4	Inhibit the growth	17 nm	*S. aureus, E. coli*	Pu et al., 2016
Chitosan	Stop DNA replication	200 nm	Staphylococcus	Silva et al. 2015
Heparin	Inactivate thrombin	250 nm	*E. coli*	Kumar et al., 2016
PMLA	Hydrolytic Degradation	302 nm	*S. aureus, E. coli*	Arif et al., 2018
SLNs	Defuse In Cell Membrane	133 nm	*MRSA*	Kalhapure et al.,2017
PEG	Reduce protein and small molecule interaction	180 nm	*P. aeruginosa*	Yin et al., 2017
NLCS	Improve Drug Permeability	175-330 nm	S. epidermidis	Lewies et al., 2017
Dendritic MSNs	Growth Inhibition	79-160 nm	*E. coli*	Wang et al. 2016

Nanoparticles are used to design material that can stop the attachment of the virus to the host cell (Rai et al., 2016). They can also stop the entry of viruses into host cells. They can interfere with their replication process and stop them from spreading in the body (Goharshadi et al., 2020). They can neutralize viruses directly and increase the traditional antiviral treatments.

Nanotechnology contributes to the development of antiviral coating for personal protective equipment (Phuna et al., 2023), surfaces (Erkoc et al., 2021), and medical equipment. Nanomaterials with virucidal properties are designed to prevent the transmission of viral infections.

Nanoparticles are used to prepare many vaccines to treat viral infections (Kuczenski et al., 2018). The benefit of Nanovaccines is that they can deliver peptides or proteins to very specific cells which help boost the immune response and no booster dose is required (Gheibi Hayat et al., 2019). Nps also protect vaccines from enzymatic degradation, especially for mucosal vaccinations (Jin et al., 2019). They are easy to produce and have great biocompatibility and biodegradability which improve the bioavailability of antigens in vivo and influence the immune system. Memory cells are generated through these vaccines which make them successful against viral infections (Sulcuzewski, Liszbinski, Romao and Rodrigues, 2018).

AIDS is a very dangerous viral disease caused by HIV (Bekker et al., 2023). Its cure is very hard to find. Currently, in advanced medication, there are six medicine classes used to attack different stages of the virus. But these medicines are not easy to take. They have a heavy pill burden, toxicity, and other side effects. Moreover, AIDS is chronic so medication remains the whole life. So, there is a big need to develop modern technology. And nanoparticles can be used. ARV drug delivery with nanoparticles can decrease the pill's burden and toxicity of drugs. NPs can also be used to prepare vaccines against HIV (Jampilek and kralova, 2022). There are many studies conducted to evaluate the result of nanoparticles as a drug delivery system in AIDS and those studies have very good results. E.g. studies by Chioda et al (2014), Jayant et al (2015) Jaramillo-Ruiz et al (2016), and Parbossing et al (2017).

HBV is the cause of inflammation of the liver. It causes liver failure and cirrhosis, and the treatment of very high cost moreover toxicity by anti-HBV drugs is very high. To overcome these problems, many nano-therapy (interferon, pegylated IFN, lamivudine, adefovir, entecavir, telvivudine, and tenofovir) are available that have very good results. (Singh, Kruger, Maguire, Govender and Parboosing, 2017).

Virus	Nanoparticle type	Size	Mechanism Of Action
HIV-1	Silver (Ag)	1-10 nm	Interaction with gp 120
	Gold (Au)	2-20	Bind with Viral envelope glycoprotein
	Polymeric	50 nm	Inhibition of TAK-779 receptor
HSV-1	Ag	4nm	Competition for the binding of the virus to cell
	Au		
HBV	Ag	10-50 nm	Interact with DNA
Monkeypox virus	Ag	10-80 nm	Block host- virus-cell binding and penetration
Influenza Virus	Au	5-10 nm	Inhibition of virus binding to plasma membrane

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