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Review Article

Introduction about Global infectious disease and use of nanotechnology

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Abstract

Infectious diseases, including COVID-19, malaria, tuberculosis, and sexually transmitted diseases (STDs), pose significant threats to global health. Nanotechnology has emerged as a promising tool in the diagnosis, treatment, and prevention of these diseases. This review highlights the applications of nanotechnology in combating infectious diseases. Nanoparticles, such as metallic nanoparticles, liposomes, and quantum dots, have been employed in the detection and treatment of infectious diseases. Nanotechnology-based drug delivery systems have improved the efficacy and reduced the toxicity of antiviral and antibacterial drugs. Additionally, nanotechnology has enabled the development of point-of-care diagnostics and vaccines for infectious diseases. This review provides an overview of the current state of nanotechnology in infectious disease management and highlights its potential to revolutionize the field. By leveraging the unique properties of nanoparticles, nanotechnology can provide innovative solutions for the diagnosis, treatment, and prevention of infectious diseases, ultimately improving global health outcomes.

Keywords: Nanotechnology, Infectious diseases, COVID-19, Malaria, Tuberculosis, HIV/AIDS

Introduction:

Infectious diseases constitute the primary cause of mortality worldwide[1]. Infectious conditions caused by viruses (human immunodeficiency virus (HIV), hepatitis C, and dengue fever, parasites (malaria, trypanosomiasis, and leishmaniasis), and bacteria (tuberculosis and cholera) are significant contributors to morbidity and death in the developing countries[2]. Nanotechnology is a modern and innovative domain characterized by technological advances[1]. Nanotechnology is characterized as a technology employed to fabricate nanoscale materials across various domains, including materials engineering, energy, biotechnology, physics, and pharmacy[3]. It provides an incredible chance for improving drug-resistant microbial infections[1]. Furthermore, it significantly influences the treatment of global infections, as well as and health care devices such as imaging probes, drug delivery systems, and diagnostic biosensors within the pharmaceutical sector[4]. Nanoparticles (NPs) are microscopic entities made of several hundred atoms, with dimensions quantified in nanometers[5]. Nanoparticles (NPs) are solid, biocompatible polymeric entities ranging from 1 to 100 nanometers (nm) in size, characterized by an enclosing interfacial coating[6]. Nanoparticles and Nano-pharmaceuticals are classified into many types of nanosystems according to their distinct properties, namely inorganic, organic, lipid-based, polymeric, and nanocapsules, among others[7].

Organic Nanotechnology - Organic nanoparticles are the most thoroughly researched and widely accepted form of nanoparticles for drug delivery and therapeutic applications in human systems [6]. Organic nanoparticles contain polymeric nanoparticles, nanocapsules, nanospheres, liposomes, dendrimers, solid lipid nanoparticles, quantum dots, among others[8].

a. Liposomes - The term liposome is derived from two Greek words: 'Lipo', meaning fat, and 'Soma,' meaning body. Liposomes are tiny bilayer vesicles created from natural phospholipids. They may contain hydrophilic and lipophilic compounds in aqueous environments or inside the phospholipid bilayer[9].

b. Quantum Dots- Quantum dots, or semiconductor nanocrystals, have unique optical and physical characteristics that render them appropriate for diagnostic advancements[10].

c. Dendrimers- Derived from the Greek term 'dendron', signifying tree. Dendrimers are a unique category of polymeric compounds. Dendrimers are often characterized as monodisperse macromolecules

exhibiting a highly three-dimensional architecture, which confers a significant degree of surface activity and an extensive range of abilities[9].

Inorganic nanoparticles: Inorganic Nanoparticles far smaller in size than organic nanoparticles It encompasses size ranges of 1-100 nm with enhanced loading effectivenss[6].

It includes:

a. Silver nanoparticles: consist of silver atoms typically measuring between 1 nm and 100 nm. Numerous synthetic techniques have been developed to manufacture AgNP[1]. SNPs are notable inorganic nanoparticles with substantial effectiveness, mostly attributed to silver's intrinsic inhibitory and antibacterial properties, as well as its improved conductivity[6].

b. Gold Nanoparticles - Gold nanoparticles, nanorods, and nanoparticles eliminate bacterial infections by emitting narrowed laser pulses at the appropriate wavelength[1]. Gold nanoparticles (AuNPs) possess exceptional qualities, including electrical, optical, mechanical, and biological capabilities, which have garnered substantial interest in the pharmaceutical industry[11].

c. Aluminium oxide nanoparticles - The bacterial cell wall became altered at elevated concentrations of aluminium oxide (Al2O3) nanoparticles. Alumina nanoparticles are thermodynamically stable at elevated temperatures[12].

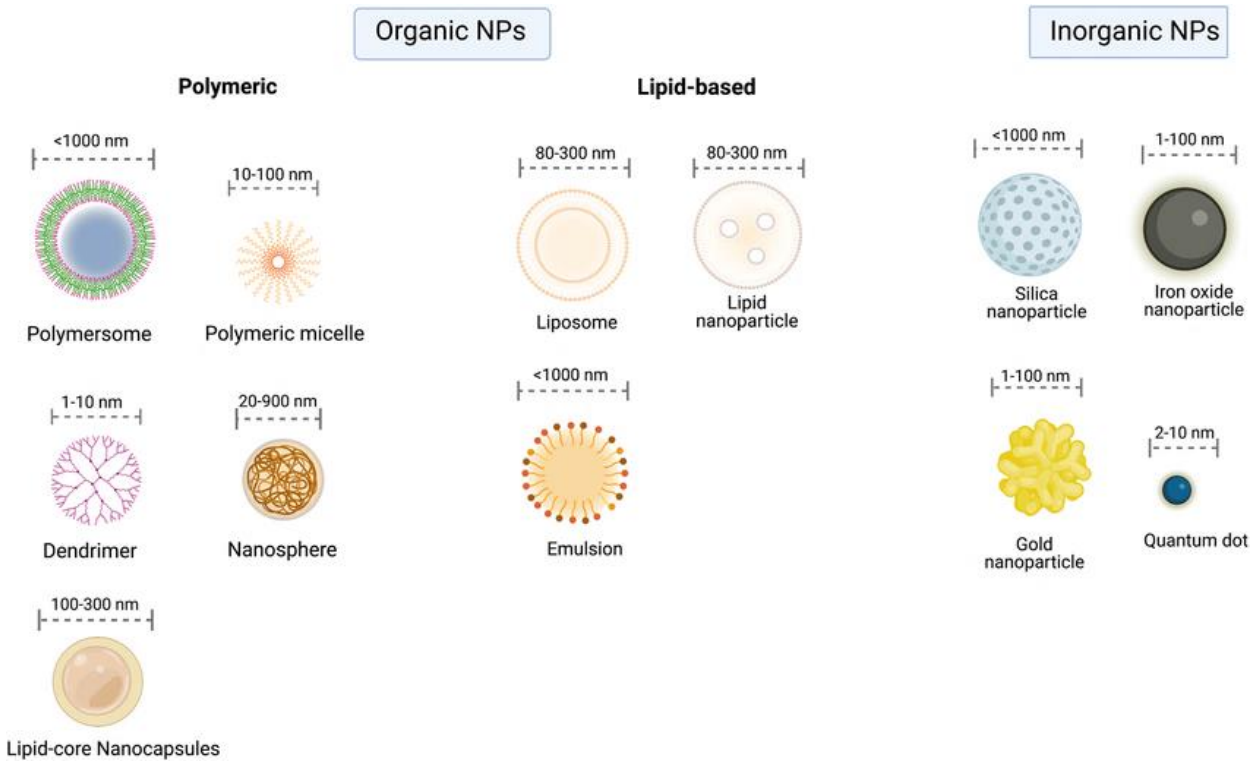

Figure 1: Various classifications of Nanoparticles (NPs) [13].

Infectious Disease –

Coronavirus –

COVID19, a severe and acute respiratory condition that originated in December 2019 and is a persistent hazard [14].

The initial case was detected in Wuhan, Hubei Province, China, and it swiftly disseminated to 25 nations[15]. Corona viruses are classified within the subfamily Coronavirinae, Order Nidovirales, including family Coronaviridae[16].

The origin of this name comes from the Latin term corona, or crown[17].

Coronaviruses (CoVs) have been among the primary causes of death in recent decades[18]. Coronaviruses are single stranded, Positive sense RNA viruses that possess the longest genome of any known RNA virus, with a genomic content (GC) varying from 32 to 43%[17].

Recent research from China indicates that COVID19, the illness produced by SARSCoV2, is characterized bythree clinical patterns: asymptomatic or mildly symptomatic cases, mild to moderate disease, and severe pneumonia necessitating ICU hospitalization[19].

The illness is spread by respiratory droplets from infected individuals during coughing or sneezing and m ostly impacts the lung parenchyma[15].

Categories of coronavirus [20].

- Alpha coronavirus
- Beta coronavirus
- Gamma coronavirus
- Delta coronavirus

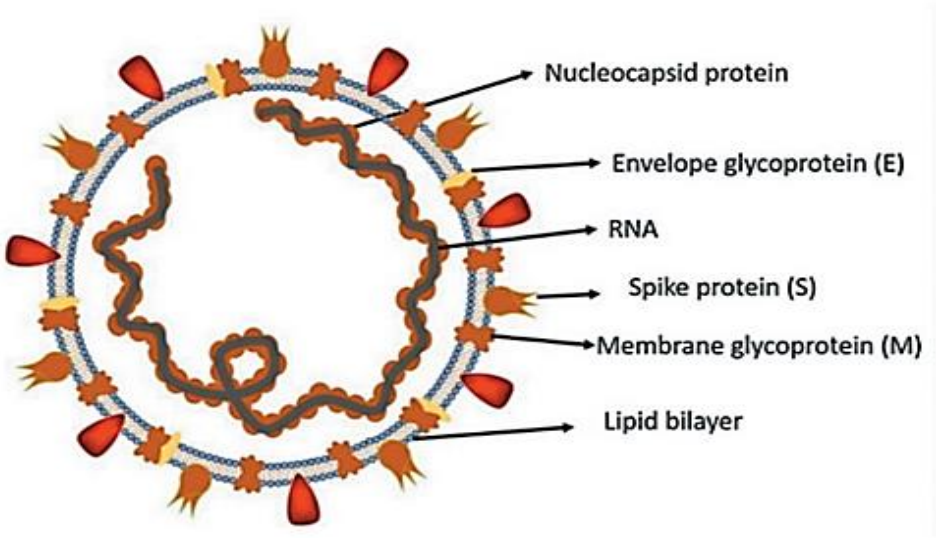

Figure 2: Structure of the human coronavirus[21].

Symptoms of coronavirus

The predominant symptoms of COVID19 are fever (85.6 %), cough (68.7%) and tiredness (39.4%). Dyspnea, headache, anorexia, anosmia, ageusia, tachypnea, emesis , diarrhea, rhinorrhea, and abdominal discomfort are less prevalent symptoms of the disease[22]. Conversely, sputum production (33.4%), respiratory distress (18.6%), pharyngodynia (13.9%), chills (11.4%), nasal obstruction (4.8%), and hemoptysis (0.9%) constitute the principle symptoms of this condition[15].

Nanotechnology Utilized in COVID-19

The utilization of nanotechnology in personal protective equipment (PPE) imbedded textiles, which enhance the physicochemical features of fabrics, including fire resistance, self-cleaning capabilities, antimicrobial effects, and UV protection, among others[23]. Nanomedicine strategies primarily aim to mitigate toxicity and adverse effects while addressing constraints associated with therapeutic agents[24].

Nanotechnology in SARS-CoV-2 Detection

The initial diagnostic stage for COVID-19 patients relies on their travel and communication history[25]. Nucleic acid-based testing was initially the principal detection method for SARS-CoV-2. Combinatorial Nanotechnology-Driven Therapy[26]. Protein assays with nanotechnology. Nanotechnology-based point-of-care testing (POCT) can be employed to identify illnesses in remote locations and deliver immediate treatment, hence aiding in the prevention of infection transmission[27].

Application of nanotechnology in coronavirus therapy

Nanotechnology may enhance the safety and efficacy of COVID-19 treatments by facilitating drug encapsulation, targeted delivery to areas, and minimizing drug toxicity[28].

Table 1: Advantages of Nanotechnology in COVID-19[1].

	Conventional Approach	Nanotechnology-based Approach
Diagnosis	Lengthy time of detection Limitations in antibody tests like technical production and identification problems Lack of suitability False positive or negative findings	Early-stage detection No or minimized contamination Protected error risk Sensitivity Possibility of miniaturization with metallic NPs NPs conjugated with corona virus specific antibodies
Treatment	Absence of effective therapeutics Low surface area to mass ratio Chemical reactivity/instability Side effects from high serum and non-target Concentrations Inaccessibility of the target by the drug	Stabilized in the systemic circulation Targeted, controlled and sustained delivery Controllable size and size-dependent transport, biocompatibility Reduced toxicity Theranostic approach Noninvasive administration like inhalations
Vaccines	Low blood stability, slow absorption and short half life Insufficient immune response Higher doses risk for side effects Poor immunogenicity, Absorption non targeting, slow absorption High storage and delivery requirements	Multiple targeting Strong immuno stimulatory effects Manageable size and surface properties Reduced adverse effects Controllable drug release Strong stimulation of humoral and cellular responses
Personal prospective equipment (PPE)	Shortage of supplies Low filtration efficiency Single-use (use-and-throw) - economic, eco-safety and waste management problems Breathing pressure and heat dissipation Ineffective disinfection and sanitizing	Reusable and improved bio-safety Self-cleaning, high efficiency and effective disinfectants with antimicrobial and antiviral properties Designing contamination-free equipment Adding inherent virucidity to surfaces Antimicrobial releasing self-sanitizing and surface topolo- gies with viral self-deactivation

MALARIA:

In 2020, there were an expected 241 million cases and 627 thousand fatalities due to malaria globally [29]. Malaria is a protozoan illness carried by female Anopheles mosquitoes, caused by the infection of a susceptible host with Plasmodium parasites[30]. The name malaria originates from the Italian phrase "malaaria," which translates to bad air[32]. The bulk of illnesses are attributed to P. falciparum and P. vivax, with the more severe P. falciparum responsible for the bulk of malaria-related fatalities worldwide[32].

Human Plasmodium species responsible for malaria[33]:

a) Plasmodium falciparum,

b) Plasmodium vivax

c) Plasmodium ovale

d)Plasmodium knowlesi

e) Plasmodium malariae

Signs and Symptoms of Malaria- The prevalent symptoms encompass fever, chills, headache, myalgia, emesis, severe anemia, spleen unresponsive coma, and mortality if untreated[34]. Malaria is the predominant etiology of fever, and the majority of patients exhibit few aberrant physical signs[2].

In uncomplicated malaria, symptoms advance sequentially through the chilly, heat, and sweating phases.

• A feeling of cold combined with shivering

• Fever, headaches, and vomiting

• Seizures may occasionally manifest in younger individuals afflicted with the condition.

• Sweating, succeeded by a reversion to baseline temperature, accompanied with fatigue[35].

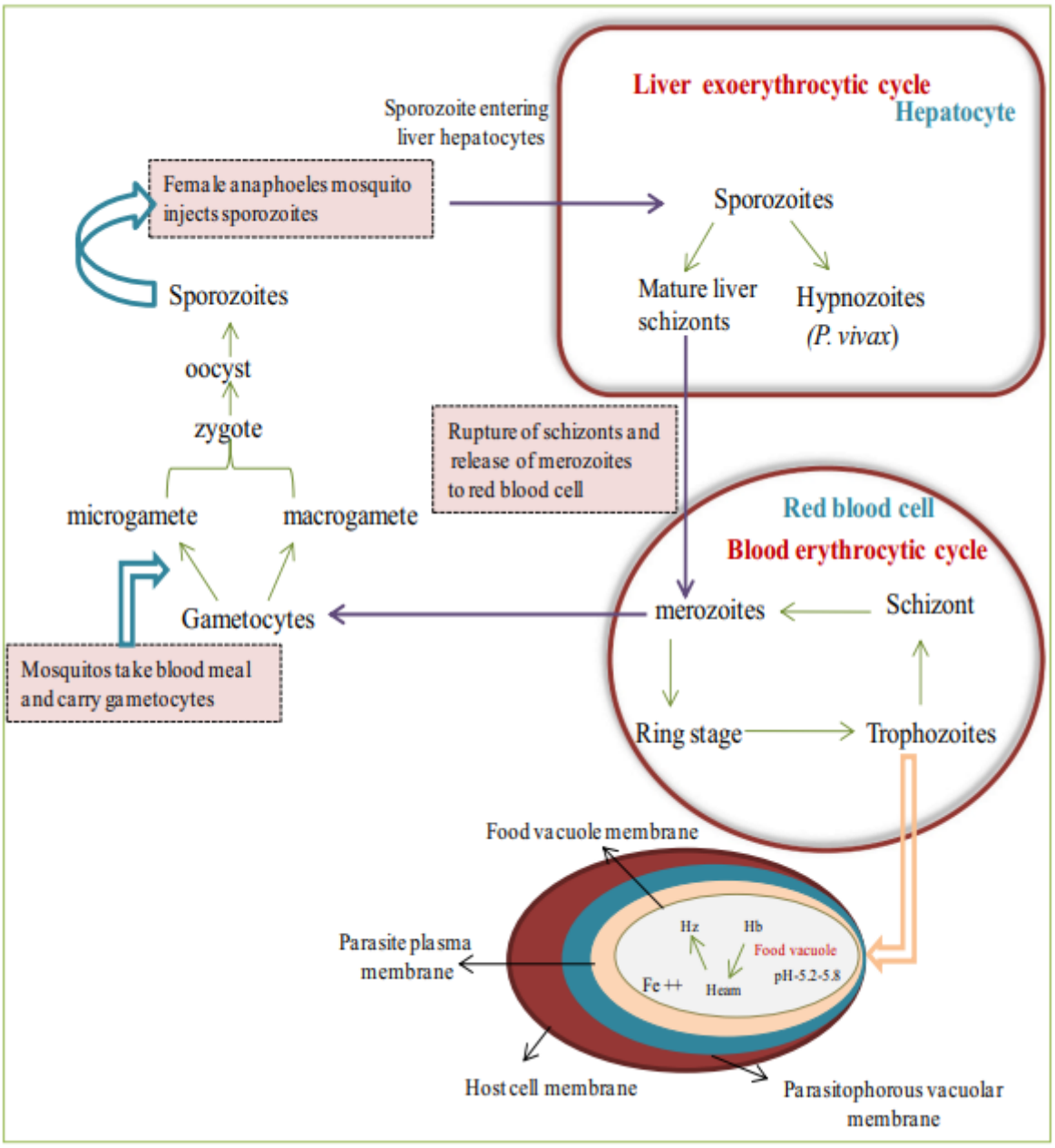

Figure 3: Life Cycle of the Malaria Parasite[34].

Techniques employed in the laboratory diagnosis of malaria encompass

1. Microscopic Diagnosis.
2. Antigen Detection Technique
3. Molecular Detection Technique (PCR).
4. Serological Detection Method (ELISA)
5. Field Assessment
6. Diagnostic procedures in the laboratory[35]
7. Rapid diagnostic assays or immunochromatographic testing - This device is recognized as a prevalent point-of-care test (POCT) for malaria diagnosis. Rapid diagnostic tests (RDTs) utilize a lateral flow immunoassay method to identify biomarkers unique to the Plasmodium parasite[36].

Application of nanotechnology in malaria therapy –

• Metallic nanoparticles - gold and silver

a. Nonbiological techniques (physical and chemical).

b. Biological Method (sustainable nanoparticles from bacteria, fungi, and plants)

• Inorganic non-metallic nanoparticles: Titanium dioxide.

a. Zinc oxide

b. Cadmium oxide[36]

• Carbon-based nanoparticles: Multiwalled carbon nanotubes.

Liposomes may transport both hydrophilic and hydrophobic medicines, exhibit great stability, are biodegradable, non-toxic, and can be delivered via parenteral and cutaneous routes. They boost the therapeutic index and allow for surface functionalization possibilities[44].

Nanoemulsions may be administered by oral, parenteral, and cutaneous routes, are thermodynamically stable, and can be sterilized using filtering.

Metallic nanoparticles have antifungal and antibacterial properties, characterized by excellent stability and uniformity in structure[34].

Nanostructured lipid carriers (NLCs) have enhanced stability and drug loading relative to solid lipid nanoparticles (SLNs), possess an extended shelf life, and facilitate straightforward scaling and sterilization. Polymeric nanoparticles are biocompatible, cost-effective, circumvent the reticular endothelial system, allow for ligand-specific interactions, and prevent drug leakage.

Solid lipid nanoparticles are biocompatible, easily scalable and sterilizable, very stable, and may be delivered by oral, parenteral, and cutaneous routes. They eliminate the need of organic solvents and can encapsulate both lipophilic and hydrophobic medicines[6].

TUBERCULOSIS –

Tuberculosis (TB) is an airborne infectious illness caused by Mycobacterium tuberculosis (MTB) that predominantly impacts the lungs[37]. Prior to the COVID-19 epidemic, more than 4,000 individuals died to tuberculosis (TB) regularly[38]

Characteristics of Mycobacterium tuberculosis: Mycobacterium tuberculosis is classified as

ORDER- Actinomycetes,

CLASS- Actinomycetes

FAMILY- Mycobacteriaceae.

GENUS- Mycobacterium[39]

Mycobacterium tuberculosis is an aerobic, non-spore-forming, nonmotile facultative bacterium characterized by curved intracellular rods.

Dimensions - 0.2-0.5 micrometers by 2-4 micrometers.

The cell walls of mycobacteria include mycolic acid-rich long-chain glycolipids and phospholipoglycans (mycolides), which safeguard them from lysosomal degradation and preserve red basic fuchsin dye upon acid rinsing, characteristic of the acid-fast stain[39,40].

Symptoms of tuberculosis [41]: Include the expectoration of mucus and sputum.

a. Fever - 74 (46.5%)

b. Weight reduction - 82 (51.6%)

c. Thoracic discomfort,

d. Jaundice: 31 cases (20.0%)

e. Diarrhea

f. Hemoptysis

g. Nocturnal hyperhidrosis

Types of tuberculosis – There are primarily two forms of TB.

a) Active TB - Bacteria reproduce and spread inside the body, resulting in tissue destruction.

b) Latent tuberculosis - This stage can last for an extended duration. Treatment typically involves administering a single medication for a duration of nine months. In active tuberculosis, germs proliferate and disseminate throughout the body, resulting in tissue damage[42].

Nanotechnology employed in the detection and treatment of TB –

Various nanoparticles, such as metallic nanoparticles (gold and silver) and fluorescent nanoparticles, can be utilized for diagnosing numerous infectious illnesses, including tuberculosis. Gold nanoparticles were the first nanomaterials employed as nano-diagnostics for tuberculosis testing in 1996[43].

Quantum Dots –

Nanotechnology employs semiconductor nanocrystals, known as "quantum dots," measuring no more than 10 nanometers, which may be induced to glow in various colors based on their size, to enhance the specificity of fluorescence or electron microscopy in detecting TB bacilli[44].

Imaging Nanotechnology –

Labeling of targeted TB-bacilli molecules with quantum dots or synthetic chromophores, such as fluorescent proteins, to enable direct examination of intracellular signalling complexes through optical techniques, such as confocal fluorescence microscopy or correlation imaging[44].

Sparse Cell Detection - This technique leverages the distinctive characteristics of sparse cells, seen in the variations in deformation of intracellular TB bacilli.

The nanotechnology-based drug delivery system enhances the tolerance of harmful chemotherapies, facilitates prolonged and regulated drug release, and ultimately increases bioavailability[42].

Exosomes are lipid bilayer membrane vesicles with a diameter ranging from 30 nm to 150 nm, released by nearly all live cells, and have a varied function in the detection and treatment of TB infection.

Liposomes: Rifampicin encapsulated in liposome nanoparticles has demonstrated enhanced anti-TB efficacy, increased absorption rate, reduced cytotoxicity, improved in vivo drug administration, and prolonged retention duration.

Noisome: Niosomes as a drug carrier, may be employed for prolonged medication delivery to minimize drug consumption and side effects by enhancing bioavailability[45].

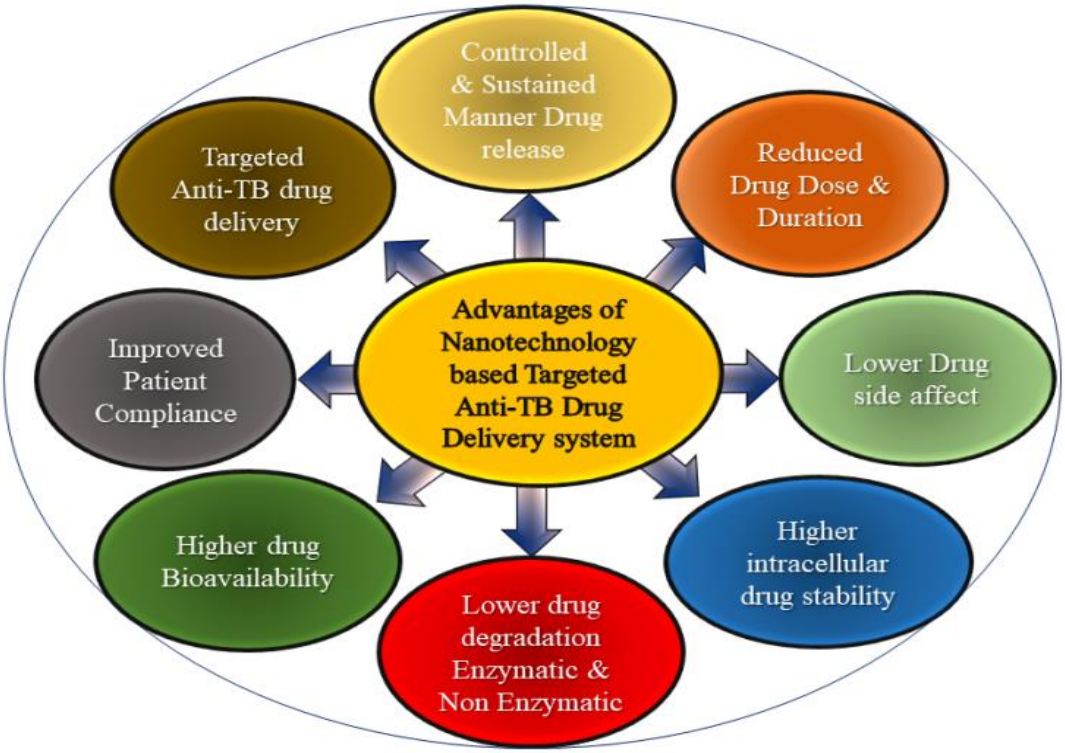

Figure 4: Nanocarrier-based anti-tuberculosis medication delivery system[46].

STD: SEXUALLY TRANSMITTED DISEASE:

Sexually transmitted infections (STIs) result in reproductive morbidity globally. In 2019, the World Health Organization (WHO) anticipated 376 million new cases of chlamydia, gonorrhea, syphilis, and trichomoniasis[47]. Sexually transmitted infections (STIs) are among the most prevalent communicable illnesses globally, linked to considerable morbidity and mortality, with a rising frequency worldwide[48].

STIs are responsible for HIV and other illnesses[49].

HIV/AIDS represents a significant challenge for the medical community, as AIDS is life-threatening and still lacks a cure, although it may be managed. The human immunodeficiency virus (HIV) is a retrovirus classified under the lentivirus family. HIV comprises a cylindrical core encased in a spherical lipid bilayer exterior.

HIV is spread through three primary methods. Sexual intercourse, exposure to contaminated bodily fluids, including sweat, tears, saliva, semen, and vaginal secretions. Vertical transfer from mother to kid during gestation, parturition, or lactation[50].

There are two strains of HIV that lead to AIDS, namely

HIV-1
HIV-2
Acute HIV infection often starts with symptoms resembling mononucleosis.

Symptoms of HIV seroconversion may encompass fever, chills, lymphadenopathy, stomach discomfort, pharyngitis, diarrhea, and rash.

Incubation duration: 2-6 weeks[51].

There are four primary phases of HIV[50].

Stage I: Clinical Latency/Asymptomatic Disease

Stage II: Mild Signs and Symptoms of HIV

Stage III: Advanced manifestations and indicators of HIV

Stage IV: Acquired immunodeficiency syndrome (AIDS).

AIDS: The human immunodeficiency virus (HIV), the etiological agent of acquired immune deficiency syndrome (AIDS), was identified more than 25 years ago. Acquired Immunodeficiency Syndrome (AIDS) is characterized by a CD4+ T cell count below 200 cells per μL or the manifestation of certain disorders in conjunction with an HIV infection[49].

Diagnosis of AIDS

1)ELISA assay,

2)Saliva test.

3)Viral load test [45].

Nanotechnology applied in HIV treatment has led to the introduction of various nanoparticle formulations aimed at prolonging the therapeutic window, thereby decreasing the required dosing frequency and addressing patient compliance issues. Stavudine, a nucleoside analogue, has been encapsulated in gelatin nanoparticles

and subsequently coated with a layer of soya lecithin-liposome for dual-functionalized HIV-1 treatment.

Virucidal nanomaterials- Various nanomaterials, including metal nanoparticles and graphene-based nanosheets, have inherent virucidal capabilities attributable to their distinctive physicochemical characteristics.

An unconventional nanoparticle platform consisting of endogenous ribonucleoprotein, known as vaults, has been utilized for HIV-1 therapy. The distinctive characteristics of nanoparticles are especially appealing for addressing several obstacles that hinder the effective practical use of RNAi antiviral treatment. Diverse tissue-targeted nanoparticle formulations, including those for vaginal administration, topical use, and cerebral distribution for neurosis treatment, have been synthesized to enhance the management and prevention of HIV infections at specific tissue locations[53].

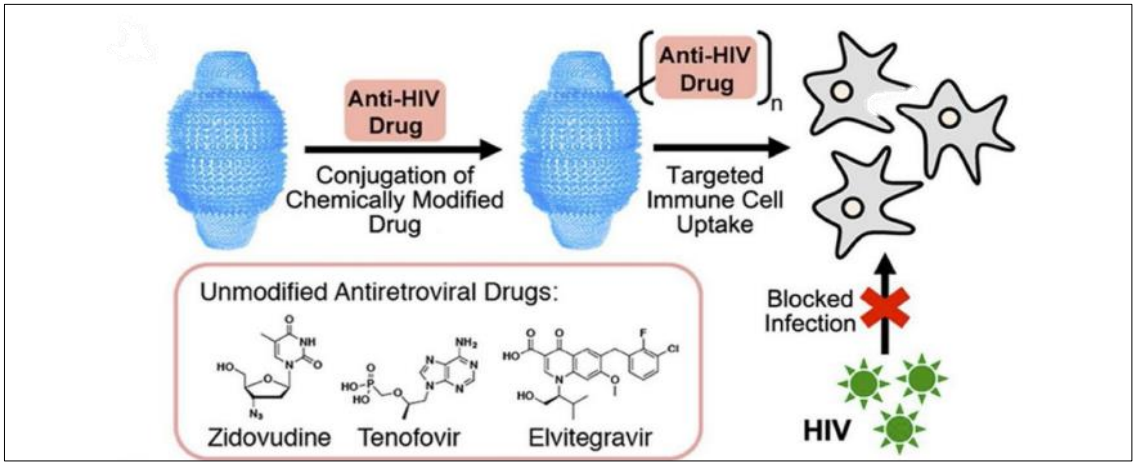

Figure 5: Antiretroviral drug-conjugated vault nanoparticles for the inhibition of human immunodeficiency virus (HIV)[53].

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