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Review Article

Nanotheranostics: A powerful next-generation solution to tackle the chronic disease

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ABSTRACT

The use of nanotheranostics is the most advanced diagnostic and therapeutic techniques for a variety of disorders like cancer, IDs, HIV has drawn significant interest in the last ten years. Currently, various methods are use in the development of bright nanotheranostics, which mix bioactive concentrating on particular tissues and diagnostic capabilities. By using nanotheranostics, keeping track the therapy responses in real-time and therapeutic drugs is delivered. As a result, there is less chance of consuming too much medication. Several non-intrusive Imaging methods have been applied to track the medication distribution processes quantitatively. Radiolabeling of nanoparticles is a popular and effective method of nuclear diagnostics imaging in medicine. Numerous nanoparticles really have been created and they have effective qualities, they were created for imaging tumors and other lesions because of their effective qualities. Multifunctional nanotheranostics have been described for inorganic nanoparticles like gold, silver, silica-based nanomaterials, or organic nanoparticles including polymers, carbon-based nanomaterials, and liposomes. A summary of the most recent nanotheranostics organized according to the utilized nanomaterials is provided. Finally, as material scientists who work in the field of nanotheranostics can use this review as a guide to create newer and more effective nanotheranostics, it can be advantageous to the medical and pharmaceutical communities as well as of society.

1. Introduction

Nanomedicine is a branch of nanoscience and also developing field combination with nanoengineering and nanotechnology, nanoparticles size range is 1 to 100 nm.[1,2] There are a number of nanomedicine backgrounds; however, nanotechnology-based drug delivery systems because nanoimaging agents are of greatest interest.[3]

Theranostic drug delivery systems are attractive platforms that incorporate diagnostic and therapeutic agents for simultaneous imaging and therapy in a single environment. Therapeutic system could aid in non-invasive monitoring of both disease progression and nanoparticle delivery pathways,[4] Theranostic nanomedicine includes the utilization of theranostics with nanosizes and numerous capabilities such as targeted drug delivery, sustained/controlled release, greater transport productivity by means of endocytosis, stimuli responsive frameworks and the combination of therapeutic approaches such as multimodality determination and treatment,[5] Theranostics refers to the pairing of diagnostic biomarkers with therapeutic agent,[6]

Such nanotheranostics are Polymer nanoparticles (NP),[7] dendrimers,[8] liposomes,[9] carbon-based nanomaterials,[10] metallic or inorganic Nanocarriers[11] and systems that integrate both categories, namely H. Polymer-coated nanocarriers.[12,13] Carbon Carbon nanotube-based nanomaterials (alone) or decorated with other materials,[14,15] graphene oxide,[16,17] fullerenes, carbon

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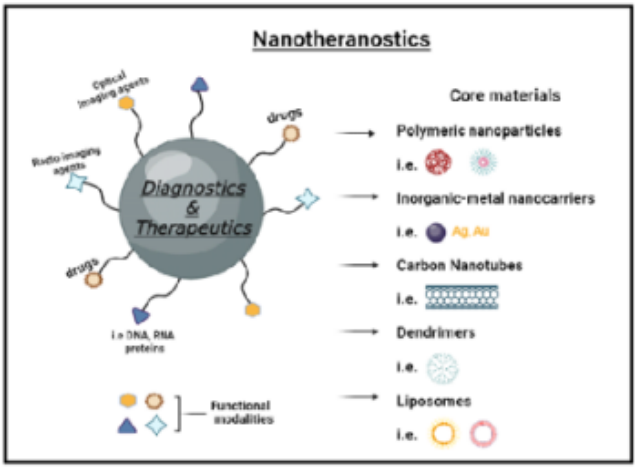

Figure 1: A schematic illustration of nanotheranostics employed for simultaneous release and imaging in preclinical settings. Drugs, DNA, RNA, and imaging agents are examples of functional groups for nanotheranostics, while polymers, inorganic and carbon-based Nano carriers, dendrimers, and liposomes make up their main structural components.

quantum dots[18] used to detect drugs in biological samples. Their imagery Prussian blue dice are octahedral metal Hexacyanoferrate developed for detection Tools with conductive and magnetic properties.[19,20] An ideal nanotheranostick should circulate for a period of time. It stays in the body for a long time and has a sufficient release effect, Excellent tissue target specificity and permeability, imaging Probability and high target-to-background ratio[21] Different nanotheranostics have the capacity to target diagnostic and therapeutic substances to specific disease spots while minimizing unwanted side effects. Their longer blood circulation time is because of their smaller nanometric size. In contrast to multi functional small molecules or functionalized macromolecules, nanosized particles can easily diffuse from the circulation into tumor tissues and be retained as a result of inadequate lymphatic drainage in the case of nanotheranostics applied for tumor diagnostics and therapy.[22,23]

Currently, aggressive therapy and innovative, forward-thinking applications in diagnostics have been sparked by nanomedicine. However, it is still crucial to create new technologies with enhanced imaging capabilities that can help with illness early detection. Additionally, imaging agents are advantageous for the medical community since they may effectively detect cancer in its early stages. In addition, nanotherapeutics is essential elements in the treatment of critical disorders.[24] However, at the moment, clinical investigations are hardly carried out, and the majority of reported NPs are assessed using data from animal models. In the past, the majority of nanotheranostics uses were for the treatment of cancer.[25] but today, nanotheranostics are used to treat diseases including neurological disorders[26] and cardiovascular diseases (CVD).[27] Have also developed Theranostics have been applied gradually to CVD with positive results.[28]

2. Discussion

Nanotheranostic Classification Based On Chemical Nature:

Currently, there is a critical need for early disease diagnosis and detection. The use of non-toxic contrast chemicals that may circulate in the body for an extended period of time in order to offer quick and accurate imaging of the lesions is one of the key obstacles to the development of effective nanotheranostics.[29]

Theranostics based on nanotechnology are divided into organic and inorganic chemical categories in this review. Whereas calcium phosphate, iron oxide, and metal- and silica-based NPs are the most frequently encountered inorganic nanotheranostics, Lipid, polymers, micelles, and carbon compounds are the most frequently seen organic nanotheranostics.

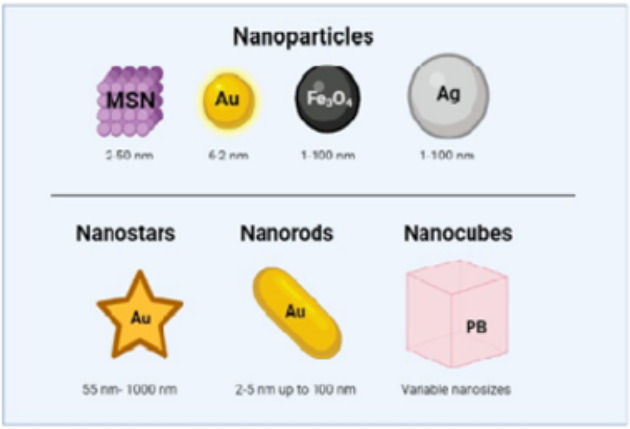

Figure 2: The use of inorganic nanoparticles as nanotheranostics is illustrated by numerous examples. Au stands for gold, Ag for silver, MSN for mesoporous silica nanoparticles, and PB for Prussian blue.

2.1. Inorganic-metal and carbon based nanoparticles

Inorganic NPs have previously produced excellent outcomes when used as drug carriers or diagnostic tools (Figure 2) although it was once believed that inorganic NPs were more stable than organic NPs. MSN exhibit a solid framework with particles ranging in size from 50 to 300 nm, internal porosity (pores with a diameter of 2 to 6 nm), a high pore volume, and organised pore networks. They have a high loading capacity, excellent cytocompatibility, and can be easily modified.[30,31]

One of the most popular gold nanoplatforms used in medication delivery is spherical gold NPs. use of gold nanorods in photothermal and NIR applications.

Through the use of Raman spectroscopy, gold nanoantennas loaded with cetuximab were demonstrated to be an effective nanoprobe for in vivo tumor identification. Raman spectroscopy relies on the variation of light frequency caused by inelastic scattering by molecules or atoms to produce fingerprint data about molecular environment or structure. The nanosystem demonstrated the capacity to specifically target cancer indicators including epidermal growth factor receptors. The created nanosystem displays strong raman signal in mouse tumors or malignant cells. The authors claim that epidermal growth factor receptors are easily bound by nanoantennas, preventing the epidermal growth factor protein from reaching cancer cells and inhibiting the signaling cascade, which stops the proliferation and survival of the targeted cells.[32]

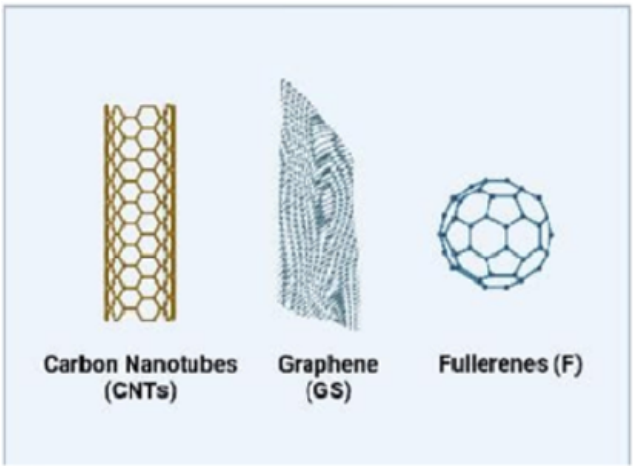

Figure 3: Nanomaterials made of carbon are utilised to make diagnostic and detection equipment**.**

In terms of biological applications, particularly in nanotheranostics, carbon-based nanomaterials (Figure 3) such fullerenes, carbon NPs, carbon nanotubes, graphene, and nano-diamonds have made significant progress.[33] Carbon nanotubes are highly organized, pseudo-one-dimensional carbon allotropes that can be either single-walled (SWCNTs) or multiwalled (MWCNTs). SWCNTs are single layers of rolled-up graphite tubes with a diameter of 0.3-2 nm, They represent an important class of theranostics because of their simple production and intriguing structure, which makes it simple to couple them with active molecules or polymers.[34] However, it is quite difficult to track them in real time.

Dendrimers, liposomes, and polymers as nanotherapeutics

Nanotheranostics have been used with a variety of polymeric, liposomal, and dendritic formulations (Figure 4). In order to enhance the inorganic particles' characteristics, delay their clearance, and reduce their toxicity, they can be coated. Yet they can also be utilized as the foundation for

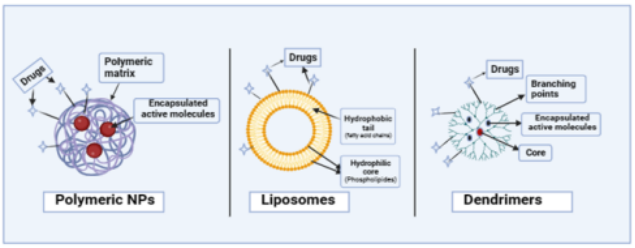

Figure 4: Various nanotheranostics layouts based on polymeric NPs, liposomes, and dendrimers.

fluorescent and drug design[1,2]

2.2. *Polymeric nanoparticles*

Due to their crucial properties, such as biocompatibility, biodegradability, and durability against degradation, polymers are among the most convenient and affordable carriers.[1] Both artificial and organic macromolecules have been used in nanotheranostics. However, in the majority of situations, they must first be altered in order to have imaging capabilities and therapeutic activity.[30] Chitosan is a basic linear polysaccharide with several desirable characteristics, including low toxicity, cost effectiveness, antibacterial activity, antioxidant capabilities, etc.[33–36] Chitosan is a polymeric core matrix that can be utilized in nanotheranostics as a coating agent.

2.3. *Liposomes*

Liposomes are organized lipid carriers that are both biocompatible and biodegradable. The FDA has approved a few liposomes.[37] Liposomes are made up of an aqueous core and one or more layers of lipids, either synthetic or natural. They have served as transporters for a variety of active compounds, both hydrophilic and lipophilic [38,39]. There are medicinal, monitoring, and diagnostic uses for radio-labeled liposomes that include radionuclides like 67Ga, 111In, and 99mTc. These liposomes are a great tool for selecting the most effective treatment action for certain patients, in addition to their imaging capabilities brought on by the radio-labeling. Iminothiolane-Tc-tricarbonyl compound was used as a model liposome system by a research team and radiolabelled. The liposomal medications Epaxal ® and Inflexal V ®, which have FDA approval, are mimicked by the system.[40] The majority of the time, active compounds like PEG or vitamins is used to functionalize or coat liposomes, which can increase their biocompatibility. For instance, TPGS-coated liposomes containing vitamin E are frequently made.[41] dditionally, as cancer nanotheranostics, PEG-coated and folate-PEG-coated long-circulating and pH-sensitive liposomes loaded with 159Gd and poly-l-lysine were investigated. Increased animal survival and significant tumor uptake are provided

by the produced liposomes.[42]

2.4. Dendrimers

The most important nanostructured materials are dendrimers because of their exterior groups, which can be altered by proteins, peptides, or antibodies. The Greek word "dendro-tree" gives its name to dendrimers, which have a structure resembling a tree's limbs or branches.[43]

3. The Stability of The Nanoparticle-Drug Complex

The clearance rate via renal excretion and interactions with the RES determines blood circulation times. Smaller nanoparticles are quickly eliminated by the kidneys, whereas larger ones are eliminated by the RES. The systemic bioavailability of nanoparticles is decreased when they are entrapped by cells of the RES. In contrast, surface modification with hydrophilic PEG chains can give nanoparticles "stealth-like" properties, prolonging their stay in the bloodstream by lowering their immunogenicity and preventing mononuclear phagocytic cells from recognizing and engulfing them.78 Additionally, PEGylation of nanoparticles acts as a biological layer to improve stability and prevent possible protein adsorption and aggregation since "naked" nanoparticles adsorb proteins, which causes them to aggregate in biological media. This helps keep nanoparticles dispersed in solutions by preventing their agglomeration. This stops the aggregation of nanoparticles in solution, which helps prevent them from clustering once within blood vessels, where they may otherwise embolize and obstruct blood flow, causing micro infarctions at various locations and organs.[44]

3.1. Dignosis

A variety of diagnostic tools, contrast agents, and drug delivery nanosystems have been developed over the past few years as a result of the integration of nanotools with life sciences. When compared to larger monofunctional particles, the multifunctional nanoscaled materials (Figure 5) often exhibit promising biological activity, stability, and better biodistribution. Additionally, it has been noted that ingestion of nanoparticles on cellular or intracellular surfaces correlates with the sizes and chemical makeup of the particles. NPs may generally be linked to cells if their diameters are less than 200 nm.[45] Although these nanosystems might offer supplementary data derived from various imaging agents, they don't have comparable qualities. Consequently, the imaging component of a novel Nanotheranostic system should be chosen in accordance with the desired administration route. As an example, the targeted delivery of imaging agents should be thoroughly investigated to assess the possible impacts of the targeting's specificity and any harmful side effects produced on by off-target accumulation.[1,2]

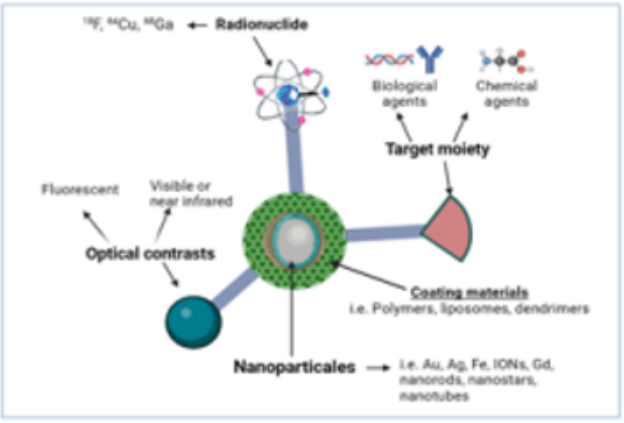

Figure 5: Multifunctional coated nanotheranostics is shown schematically in great detail. While therapeutic target groups may include both chemical and biological agents, imaging agents can be categorized on the basis of fluorescent or visible-infrared moieties, radionuclides. (The reader is directed to this article's web version for clarification on how to understand the references to color in this figure legend.)

Radiopharmacy, nuclear medicine, and radiology all use a variety of imaging methods. In radiology, common imaging methods include radiography, ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI). These techniques enable the diagnosis of numerous disorders, primarily cancer. Even so, the cancer cell will have about 1 billion cancer cells at a size of roughly 1 cm3 when it becomes visible. As a result, once the phenotypic alterations start, it would be too late to diagnose the tumor region. For effective treatment, it is crucial to identify cancer at an early stage by molecular means.

As a result, research has shifted its attention from radiological to nuclear imaging. The in vivo monitoring of biological processes at the cellular and molecular levels, as well as the genetic changes in the tissues, is referred to as nuclear medicine imaging. Additionally, it non-invasively images the pathophysiologic situation, provides details on specific molecular changes, aids in early diagnosis, identifies the disease stage, provides a basic understanding of pathological processes, predicts the course of the illness, and administers personalized medicine.[43]

The four main categories of NPs for imaging are magnetic, fluorescent, magneto fluorescent and radiolabeled. The discovery, formulation, preparation, quality assurance, and administration of radiopharmaceuticals are within the boundaries of radiopharmacy, a multidisciplinary scientific field. In order to diagnose or cure a variety of disorders, radiopharmaceuticals are medications that comprise radionuclides and pharmaceutical components.[46] The pharmaceutical component is selected based on either its preferred location within the intended organ to be

photographed or its involvement in the physiological function of the organ.

A suitable radionuclide is applied to the pharmacological component when it is chosen, and once it has been localized in the organ, it can be spotted using a variety of imaging techniques. The pharmaceutical component is chosen based on either its preferred location within the intended organ to be imaged or its involvement in the physiological function of the organ. After being chosen, the pharmacological component is labeled with an appropriate radionuclide, and once it has been localized in the organ, it can be found using a variety of imaging techniques.[47]

Numerous polymeric NP-based nanotheranostics have been created and radiolabeled utilizing a variety of techniques with the goal of aiding in the detection and treatment of illnesses. In order to increase the stability of radionuclide and NPs linking molecules such chelator agents attach to them. The characteristics of radionuclides' short, medium, and long half-lives, as well as their chemical makeup and radioactive decay, may have an impact on as an example, Theranostics properties can be found in radiopharmaceuticals that emit beta and gamma particles. To ascertain the physiological or anatomical condition of tissues, they function as both diagnostic and therapeutic tools. For directing nanotheranostic to the targeted region, radionuclide choice is crucial. When NPs are radiolabeled using gamma, beta, and alpha emitters, the NPs develop theranostic properties.[48] These emitters can also cause the imaging of cellular activity and the observation of cellular molecular processes. Because of its widespread availability, low cost, acceptable imaging capabilities, and a half-life (6 h) that allows imaging for up to 24 h, technetium-99 m is commonly used as a radionuclide to radiolabel nanosystems. Radioisotopes of iodine are the next most commonly utilized radionuclide, after indium-111. Positron-emitting radionuclides like Flour-18, Manganez-52, and Zirconium-89 have been used more frequently recently, which reflects the rising demand for preclinical and clinical PET scanners in radiopharmacy and nuclear medicine applications as well as the growing interest in positron emission tomography (PET) imaging. The energy levels of the emitters are a crucial consideration when choosing a radiation type. The β- and γ -emitters are frequently utilized because of their extensive ranges and controllable energy levels.[48]

4. Treatment

Nanotechnology in treating Infectious diseases (IDs):

For the proper treatment of IDs, safe and effective drugs must be readily available. In-depth preclinical testing has been done on nanotechnology-based methods to increase the ID medicines' therapeutic index and make their use simpler. We emphasize intriguing preclinical research and talk about obstacles to their translation for medical use.

4.1. Sustained systemic delivery of anti-infective

The supervisors of many IDs involve long-term care, which is extremely taxing on both the patient and the healthcare system. HIV-infected to guarantee that the viral infection is under control, people need lifetime treatment burden.[49] A combination of tablets must be used in order to treat TB during a period of months to years, frequently more than once day. Drug delivery for extended periods via injectable Nanocarriers has been actively sought after. These systems can be broadly divided into two groups: those that regulate drug release using an excipient (such a polymer or lipid) and those that depend on the slowly dissolving of drug crystals that are not very soluble in interstitial fluid. (Figure 6).

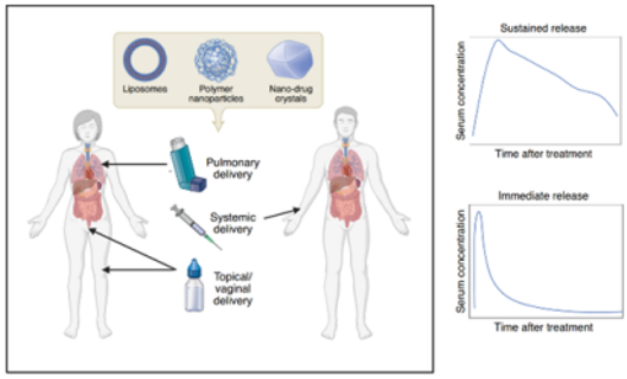

Figure 6: Nano carriers for sustained systemic and local distribution**.** Medications can be packaged in Nano carriers like liposomes, polymer nanoparticles, or manufactured drug nanocrystals to distribute medications locally over an extended period of time (see image at left). Treatment of local infections of the female reproductive system, lungs, and skin has been tested using these methods. Additionally, injectable Nano carriers for systemic medication delivery are being investigated (right).[50]

Medicines can also be loaded into liposomes, which are lipid vesicles with the ability to hold both hydrophobic and hydrophilic medicines, to achieve sustained release. The liposomal version of amikacin14, a medication that needs regular dosage and ongoing therapeutic monitoring, was created by NeXstar Pharmaceuticals and is known as MiKasomes.

In a rat model, Mikasomes that were given intravenously diffused throughout a number of tissues and released the drug over time, increasing the half-life of the medication by eight times. Despite early successes in clinical tests for Mycobacterium infections and urinary tract infections,[51] the formulation's development was stopped in 2000.

4.2. Local delivery

Local medication delivery to epithelial surfaces has significant potential because these surfaces are frequently used by infections as entry points and places to live. Local distribution to the infection site is believed to

improve on-target antibiotic exposure compared to systemic administration. Of course, its applicability to systemic illnesses is restricted. Numerous benefits of employing Nano formulation for local therapy have been revealed by preclinical investigations, mostly in rats. Drug delivery can be sustained with Nano carriers, which lowers the need for frequent dosage. Nano carriers can be designed to release medications only when specific triggers are present and to manage the timing of drug exposure. Medication efficacy against intracellular infections may be improved by Nano carriers by enhancing medication uptake in cells. Finally, encapsulating labile pharmaceuticals (such nucleic acids) in Nano carriers may shield them.

4.3. Vaginal drug delivery

The vaginal tract is a route of entry for both HIV and the herpes simplex virus (HSV). By administering microbicides locally as a preventative measure, infection risk can be decreased. Maximal coverage of the entire vaginal tract at the time of infection is likely to reduce the likelihood of infection. Complete vaginal coverage and sustained residence of the medication delivery system are restricted by a number of factors.[52] Following the use of a medication delivery system, formulations may first leak out of the vaginal tract.

Second, a coating of mucous, a viscous biopolymer comprised of glycoproteins called mucins that covers the vaginal mucosa and functions as a diffusional barrier to trap drug particle matter, is present.

Third, because the mucous layer sheds so regularly, particles caught within of it may be lost. Fourth, there are numerous folds or rugae on the vaginal surface that prevent easy medication access. Finally, vulnerable medications may be destroyed by the vaginal fluid's low pH and enzyme content.[52]

4.4. HIV infection

One of the main IDs causing high rates of illness and death worldwide is HIV infection. HIV impairs the patient's immune system, providing them less immune to accidental infections. It predominantly targets CD4+ T cells.

The most innovative nanotechnology for HIV treatment is found in long-acting injectable antiretroviral. The reduction in dose frequency caused by long-acting injectable nanoparticles should increase patient compliance. They also permit the administration of medications to patients with dysphasia, such as those who are HIV-positive and have opportunistic esophageal infections. Additionally, there has been some interest in creating long-acting nanoparticles for prevention, particularly for pre-exposure prophylaxis, which calls for the continuous administration of two medications to provide protection, and post-exposure prophylaxis, where the administration of a single injection or long-acting oral medication would be particularly beneficial. The clinic is aggressively pursuing the use of nanoparticles of two antiretrovirals, cabotegravir and rilpivirine. Due to their effectiveness at low oral dosages and limited water solubility.[53]

Clinical studies have assessed the pharmacokinetics, effectiveness, and safety of rilpivirine and cabotegravir nanosuspensions (drug nanocrystals with surfactant stabilization with a mean diameter of 200 nm). Both nanosuspensions were secure and free of significant negative effects. Rilpivirine and cabotegravir's estimated half-lives in nanosuspensions were 44–61 days and 25–54 days, respectively, allowing administration every one to three months. Rilpivirine and cabotegravir's half-lives in tablets, however, have been calculated to be between one and two days. Rilpivirine and cabotegravir nanosuspensions were used in Phase IIb clinical studies to achieve disease suppression comparable to cabotegravir and abcavir-lamivudine oral tablets.[54]

However, additional research could be needed to verify this observation. Clinical trials for the production of efavirenz and lopinavir nanoparticles are now being prepared (NCT02631473).

5. Nano Imaging Application for Cancer

There are two types of nanotheranostics for cancer: conventional and biomimetic.[55] Traditional Nano carriers with considerable potential as anticancer treatments include liposomes, micelles, Nano gels, and NPs. However, due to the requirement that they be successfully coupled with fluorescent dyes or other active molecules before usage, their utility as imaging or diagnostics is restricted. Additionally, these systems ought to be functionalized with substances like (polyethylene glycol), or PEG, which might lengthen circulation times. Since they can combine the biological functions of biomimetic compounds like proteins, phospholipids, cholesterol, cell and cell membranes, pathogens as bacteria and viruses and other pathogens, apatite, and exosomes, biomimetic nanosystems as nanotheranostics have attracted researchers' attention.[56] The increased permeability and retention (EPR) effect, which states that NPs tend to accumulate in tumor tissue much more than they do in normal tissues, is the foundation of the current cancer Nano therapeutics. Drug delivery to the tumor site is constrained by the fact that this phenomenon is dependent on the microenvironment of the tumor and is not consistently seen in all tumor types. Therefore, tumors or more therapeutically relevant cancer models should be employed to study cancer nanotheranostics.

5.1. Future aspects

Overall, nanotheranostics has demonstrated considerable promise in the detection and management of chronic

disease. Although functional nanosystems have made significant advances in the detection, treatment, and prevention of various diseases, this research area is still in its early stages and demands multidisciplinary collaboration, as well as the combination of chemistry.

The development of infectious disease a major contributing factor too many diseases, in order to treatthese diseases in use theranostic treatments. They have also been shown effective at targeting specific molecular targets, such as enzymes, receptors, and proteins, which can be used to identify and target disease-causing cells.

6. Source of Funding

None.

7. Conflict of Interest

None.

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