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Emerging Nanotechnology Approaches for HIV/AIDS treatment and prevention

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Abstract

Currently, neither a vaccine nor a treatment exist for HIV/AIDS. Combination antiretrovirals have greatly improved treatment, but they must be used for the remainder of one's life, have harmful side effects, and are ineffective in patients whose viruses develop resistance to them. The trans disciplinary science of nanotechnology is transforming medicine in the twenty-first century. It could make substantial advancements in HIV/AIDS treatment and prevention. We discuss the shortcomings of the disease's current treatment in this assessment and draw attention to the tremendous potential of nanotechnology to provide more effective anti retro viral medication, gene therapy, and immunotherapy for HIV/AIDS treatment and prevention, microbicides, andvaccine.

The particle can enter thebody mostly through inhalation, direct injection, and oral in take.It has proven to have the potential to enhance viral agent treatment and prevention. Numerous NPs tested in vitro for self-therapeutic activity against the virus.

Key words: Nanotechnology, HIV, Vaccine, Nanomedicine, Antibodies

Introduction

Currently, there is no effective medication available to treat the HIV infection, which affects approximately 37 million people worldwide. There are two main types of the virus: HIV-1 and HIV-2. The study focuses on HIV-1 therapy possibilities since it is more prevalent, damaging, and preferentially infects CD4+ Tcells, helping cells. HIV-1 can infect macrophages, dendritic cells,
and other types of cells. High-dose antiretroviral therapy (HAART) is an effective HIV-1 treatment strategy, but it does not provide patients with a functional or sterilising cure because the mechanisms of infection for microglia and astrocytes have not yet been fully identified and understood. Additionally,a number of adverse comorbidities are brought on by HAART (highly active anti retroviral therapy). As highly active antiretroviral treatment (HAART) focuses on the
HIV-1 enters a state of latency during its replication cycleo avoid being targeted. HIV was first identified as the disease's a etiology in 1983, after which AIDS's beginning had been detected in 1981. Today, HIV/AIDS is the most prevalent infectious disease in the world that kills adults. By 2006, more than65 million people had acquired the HIV virus globally,and25 million had died from AIDS. By the end of 2007, the virus had infected about 33 million people, and it was responsible for 2 million fatalities annually. Particularly on developing nations in Sub-Saharan Africa, this has had a tremendous detrimental social and economic impact on the entire world.

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Nanotechnology for HIV/AIDS treatment

Similaradvantagesmightbeprovidedbynanotechnology-basedplatformsthatdistributeantiviral drugs throughout the body. Controlled-release delivery systems can extend their half-lives, keeping them in the bloodstream for longer periods of time at therapeutic concentrations. This might significantly improve adherence to medicine. Nanoscale delivery techniques enhance and control the distributionofhydrophobicand hydrophilicdrugsintoandthroughout diversetissues due to their small size. This specific feature seems to be the most promising component of nanoscale delivery systems for the therapeutic treatment and prevention of HIV.

In a recent study, dogs and mice were given nanosuspensions (200 nm) of the drug dipivefrine (TMC278) stabilized by polyethylene-polypropylene glycol (poloxamer 338) and PEGylated tocopheryl succinate ester (TPGS 1000). polymeric systems-based study [35]. A single dose of the medicinegiven in nanosuspensions generatedsustained release over 3months in dogs and 3weeks in mice, compared to a half-life of 38 hours for free medication. These results demonstrate the potential for nanoscale medicine delivery toincrease adherenceand decrease dosing frequency.

Types of Nanoparticles and Nano pharmaceuticals:

Liposomes, Micelles, Nanospheres, Nano capsules, Organic Nanoparticles, Polymeric Nanoparticles, Dendrimers SolidLipidNanoparticles,second

1. Silver nanoparticles (SNPs) and gold nanoparticles (GNPs) are examples of inorganic nanoparticles.
2. Organic nanoparticlesare the type of nanoparticle that have been the subject of the most research and are the most commonly approved for use in the delivery of medicationsand for therapeutic purposes in human systems. The most common varieties of organic nanoparticles include nanoparticles made of polymers - Sizes of polymeric nanoparticles, which are solid colloids, range from 10 to 1000 nm. Higher concentrations at the target areas are the result of smaller size, which enhances capillary entrance and cell absorption. In order to serve as therapeutic providers, NPs made from biodegradable and biocompatible polymers have received extensive research. those employed in pharmacology and medicine The WHO and FDA have approved polyglycolides.poly(PGA),polylactides(PLA),andLactide-coglycolidepolymerBecauseofits outstandingpotentialforbiocompatibilityandbiodegradation,poly(D, L-lactide-co-glycoside,or PLGA) (PLG)- based nanoparticles are used extensively. The effectiveness and security of the drugs they contain can frequently beimproved bythem. It fallsinto the category ofnanospheres or nano capsules.

NanocapsulesincludeNanocapsulesarespherical hollowshereswithpolymercoatingswithin, and they havea size range of50 to300 nm, a high loading capacity,and a low density.

Thesenanospheres:Theyhaveanequaldistribution ofthemedicationthroughoutamatrixsystem with a size range of100 to 200 nm. There have been numerous investigations onthe therapeutic potential of nanospheres for viruses other than HIV/AIDS.

The first nanoparticle (NP) platform for the delivery of genesand drugs was liposomes. Liposomes are. They are sphere-like vehicles with a diameter of 20–30 nm. It is made up of an aqueous structure at the centre ofa bilayer phospholipid structure. The interior aqueous cavity or bilayer phospholipidcanbesupplemented withhydrophilicor lipophilic drugs,respectively.Becauseof their wide range of compositional variations,ability to hold and protecta variety of varietiesofbiomolecules,aswellasbiocompatible andbiodegradablecharacteristics.Liposomal formulations are extensively researched in vaccination due to their potential as immunological adjuvants. About twelve of our liposome-based drugs are registered clinically.

Micelles:-

Thediameterofmicellesvariesfrom10to100nm.Theyconsistofaninsidewater- phobic core and an outside water-loving polymer. They are made of polymeric micelles, which are interestingbecause vehicles with high therapeutic potential for drugdelivery. Theencapsulation of

pharmaceuticals in polymeric micelles is an innovative application of nanotechnologies that can improvethewater solubilityand stability ofunstable medications.Theuse ofmicellesintherapy has many advantages, including their decreased dissociation rate, which lengthens the time that medications are retained and accumulates at the target site.

DendrimersincludeDendrimersare symmetricalmacromoleculeswhereinteractionta kesplace. They havea structureofhyper-branchesthat emergefroma central stick throughconnectorsand units of branches. The target domain management is under the purview of the terminal groups. These arespherical and have threeseparate domains. organizations operating. For groups youwant totargetmolecularly,fordetecting,imaging,andot herpurposes,theoutsidefacecouldbealtered to generate chemical functional groupings. website attachments for a therapeuticagent.

1. Solid Lipid Nanoparticles (SLNs): These are a different type of pharmaceutical delivery mechanism from the general colloidal nanoparticles mentioned above. The usage of SLNs also reaps the benefits of conventional nanocarriers while avoiding their drawbacks. For instance, a significant barrier that reduces the usage of drug delivery is mass production of polymeric nanoparticles,whereasfinancialhelpcanbegivenf or thesynthesisofSLNsandother materials.

2. Nanoparticles that are organic: Inorganic nanoparticles are far smaller in size than organic nanoparticles. The loading efficiency has enhanced with its size ranges of 1-100 nm. There are twomajorwaystocreateinorganicnanoparticles:"t op-down"techniquesthatusephysicaland/or chemical processes to shrink the inorganic nanoparticles to their typical nanosized size, and "bottom-up" techniques that gradually build the nanoparticle. The reaction conditions, in particular,canvarytheshapeandsizeofthenanopart icles,whilethechoiceofreducingagentcan alter other characteristics of the particles, such as their loading capacity and aggregation and release profiles.

GNPs, or gold nanoparticles: - GNPs are being extensively investigated as nanoparticle carriers due to their superior conductivity, flexibility in surface modification, biocompatibility, and straightforward production methods. They also have unique photophysical properties, physical and chemical features, andthe flexibility of functionalization via thiol linkages.

SNPs, or silver nanoparticles: -Because of silver'sinherent inhibitoryand antibacterial qualities as well as its increased conductivity, SNPsaresignificantinorganicnanoparticleswithef fectivenessduetotheirchemical stabilityand catalytic characteristics. efficiency, too. The main mechanism ofaction ofSNPs istherelease of silver ions, which increases the activity of antimicrobials and leads to denaturation of nucleic acids and distortion of cell membranes.

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Nanotechnology for HIV/AIDS treatment

Nanotechnology for anti retro viral drug delivery

Nanotechnologyplatformsfordrugdistributionare revolutionizinganumberoffacetsofsickness therapy. Cancer patients have so far benefited the most from this revolution because there have been significant improvements in recent decades. There are numerous FDA-approved or in- progress clinical nanoscale technologies for treating systemic cancer. This remarkable accomplishment is a result of the distinctive qualities that nanotechnology gives drug delivery systems. Nanotechnology has made it feasible to deliver pharmaceuticals that aren't very water- soluble more effectively, administer medications only to certain cells or tissues, and distribute macromolecules inside cells.

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Thisspecificfeatureseemstobethemostpromising componentofnanoscaledeliverysystemsfor the therapeutic treatment and prevention of HIV. To ensure that antiretroviral drugs reach latent reservoirs, they could be given specifically to CD4+ T cells, macrophages, the brain, and other organ systems. By controlling the release profiles of the delivery systems, drugs might also be administeredtotheintendedtargetsforalongerdura tionandathighereffectivedoses.Toachieve these objectives, many nanoscale drug Delivery methods similar to those in Figure 1 might be looked at. Amiji and Nowacek et al. have thoroughly assessed the use of nanotechnology systems for the delivery of antiretroviral drugs.Thissectiononlyhighlightsasmallnumber ofthemostrecentand notableapplicationsof nanotechnology in drug delivery.

Nanomaterials as medical tools

Although nanomaterials are used as delivery systems, it has been shown that they also possess therapeuticqualitiesontheirown.Studiessuggestt hatdevelopingdrugsbasedonthestructureof the HIV capsid could stop viral replication. The result is

In computational and experimental study, compounds have been identified that may hinder the HIVcapsid'selaboration.Severalfactorshavebeen foundtopreventinvitroviralreplication.Itis believedthat theeffects

ofnanomaterialsonviralassemblyarecausedbystructuralinterference.

Genetherapy for HIV/AIDS

In addition to efforts to find new HIV/AIDS treatment alternatives, existing antiretroviral medicationsare being enhanced. Agene isinserted into a cell aspart ofthe potential alternative methodknownasgenetherapytostopviralinfection orviralreplication.Othernucleicacid-based compounds, such as DNA, siRNA, RNA decoys, ribozymes, and aptamers, as well as protein- based compounds, such fusion inhibitors and zinc-finger nucleases, can be used to stop viral proliferation.

In the early stages of gene therapy for HIV/AIDS, viral vectors were the main delivery method used;certain clinical trials are currently underway. Benitec Ltd. and City of Hope are collaborating on one of these studies to examine the viability and safety of a gene therapy strategy based on a single lentiviral vector that leverages stem cells for delivery and combines three different inhibitory genes. UCLA researchersrecently showed that cell-derived gene transfer is both safe and biologically beneficial in HIV-infected persons in a Phase II clinical trial of gene therapy. These programmes encourage and support the growing interest in gene therapy as a potential treatmentforHIV/AIDS. However, lessonslearned overthepasttwodecadessuggestthattheuse of viral vectors for gene delivery may bring fundamental problems such as toxicity, immunogenicity, insertion mutagenesis, and limitations with scale-up techniques. These problems have sparked research into nonviral vectors for gene delivery, a field where nanotechnology platforms appear especially promising.

MechanismforsiRNA-basedgenetherapyofHIV/AIDS

ThesiRNAdegradesmRNAinatleasttwodifferent ways:(A)bypreventingthe developmentof receptorsorco-receptors,whichlimitsentryandfusion;and(B)byobstructingthetranslationand transcription of viral genes, which obstructs the production of proteins and genomic RNA. (The viral entrance and replication stages listed below are the targets of the antiretroviral drugs.)

Similar to other genetherapytechniques, the challenge ofdelivering siRNAto specific cellsand tissues has significantly impeded the use of RNAi. New nanotechnology platforms that provide nonviral replacements for effective and secure delivery are addressing this issue. Self-assembling, cyclodextrin polymer-based nanoparticles for the first nontargeted administration of siRNA in human phase I clinical studies just got going.

NonviralsiRNAdeliveryforthetreatmentofHIVinfectionisprogressing,albeitbeininitsearly stages. A fusion protein with apeptidetransduction domain anda doublestrandedRNA-binding domainwasusedtoencapsulateanddeliversiRNAtoTcellsinvivo.WhensiRNAstargeting CD4 andCD8 weredelivered,theRNAiresponsesthatresulted had noadverseeffectsrelatedto cytotoxicity or immunological activation. Similar to this, it has been demonstrated that siRNA administrationusinga protamine-antibody fusion protein can stop HIV replication in primaryT cells.

Ithasbeenshownthatsingle-walllednanotubescandeliversiRNAspecifictoCXCR4andCD4to human T cells and peripheral blood mononuclear cells. CXCR4 receptors were shut down on T cells.CXCR4receptorsonperipheralbloodmononuclearcellswereknockeddownbyupto60%, CD4 expression was decreased by up to 90%, and vice versa. In a different work, amino-terminated carbosilanedendrimerswithinternalcarbon-silicon connectionswereusedtotransport siRNAto HIV-infected cells.

Immunotherapy for HIV/AIDS

Thevarioustherapyapproacheslistedaboveeither specificallytargetHIVatthelevelofthehost cellorthevirusitselfinordertoeffectivelycureHIV/AIDS. Analternativemethodthatalterstheimmune system's reaction to HIV is immunotherapy. CD8+ cytotoxic T-cell responses to acute HIV infection appear to be quite normal, despite the fact that B cell production of neutralizing antibodies is either delayed or nonexistent. Viral mutation causes

CD8+ T lymphocytes to lose their capacity for cytotoxicity over time. The primary effect of HIV infection is, however, the reduction in CD4+ T cells. When these "helper" T cellsare lost, significant immunosuppression results, which is visible in people with chronic HIV infection.These "helper" T cells play anumber of supportive roles for other immune populations. characterized by the presence of aberrant macrophages,naturalkillercells,andB-cells.Inrecentyears,increased focushasbeenplaced on the therapeutic use of immune responses to restore the immune system's regular operation as an effectiveHIV/AIDS treatment. There ismounting evidence thattheimmune system may beable to regulate HIV in some individuals. Techniques that restore or enable the restoration of immunological function maytherefore be among the finest means of effective treatment.

Immunotherapy is the use of immunomodulatory medications to modify the immune system's responsetoadisease.Byimmunizingpeoplewithvarious immunologicformulations,itfunctions similarly to vaccinations but treats HIV-infected patients rather than protecting the healthy (preventive vaccines will be covered in a forthcoming article). section). The foundation of the variousHIV/AIDSimmunotherapytechniquesmaybethedeliveryofcytokines(suchIL-2,IL-7, andIL-15)orantigens. APCsarerequired forthedevelopment ofboth cellularimmunityand, to asignificantextent,humoralimmunity. APCsprocessandpresentantigenstoCD4+andCD8+T cells.Dendriticcells(DCs),themodelofaprofessional APC, startanddirectthedevelopmentof cellular and humoral (antibody) immunity. Then, protein/peptideantigens or DNA immunogens couldbedeliveredbyviralvectorstoendogenousorexvivo-producedDCs,resultinginthe generation of endogenous proteins.

Nanotechnology for HIV/AIDS prevention

Thesearchforarisk-freeandefficientHIV/AIDSvaccinehasbeenchallenginginthenearlythree decades since the disease was identified. Many debates over vaccine development have been ignitedbyrecenthigh-profileclinicaltrialfailures,withsomesayingthatthereshouldbeagreater emphasis on fundamental research and less on clinical trials.

The key challengesin developing a preventive HIV/AIDS vaccine have been the extensive viral strainandsequencevariety, viralevasion ofhumoraland cellularimmuneresponses,aswellasa lack of methods to produce widely reactive neutralizing antibodies and cytotoxic T cells. To display protein antigens to CD4+ T lymphocytes (extracellular antigen in MHC class), protein antigensmustenter APCs(likeDCs),wherepeptidesaredigestedandloaded.II)toinduceT cell responses(intracellular antigenin MHC classI) and CD8+ T cells.It is challenging to distribute exogenous antigens (likenanoparticles)toAPCsbecause theyrequirespecial"cross-presentation" in order to be presented by MHC class I and activate CD8+ cytotoxic T cells. The need for cytosolic delivery of antigens and cross-presentation is another barrier to the development ofan intracellular HIV antigen vaccine, while this may be a benefit of nano delivery. It is difficult to elicitjustonecellularorhumoralreaction;rather,itisdifficulttoelicitboth.Inresponsetointact antigens that are displayed on the surface of viruses or nanoparticles, hematopoietic responses (neutralizing antibodies produced by B cells) are produced. However, CD4+ T cells frequently need to "assist" these humoral reactions.

Implication of nano particles in HIV/AIDS therapy

Patients were hadtotakeupto40 drugs per day whenthisdisease was first beingtreated.It now onlycallsfora fewmedicationsperdaybecauseofadvancementsanddevelopmentsdevelopedin thelast several decadesoftreatment. It hasbeen demonstrated thatan enhanced way for making therapy effective and long-lasting is the synthesis of nanoparticles with polymers that can transport ARTtherapiestothesystemsandbraincells.Inessence,ARTdrugsaredividedintogroupsbased on

the stages of the viral agent's life-sustaining replication cycle. A combination treatment plan known as HAART is utilised to actively halt the transmission of HIV while preventing drug resistance. Antiretroviral drugadministration has greatly benefited from nanotechnology, and in expanding conformity rates. Lymphatic tissues are frequently HIV-loving and infection sites. Accordingtoresearch,ARTdrug-loadednanoparticlesspecificallytargetedinvitromacrophages and monocytes. Nanoparticle technology has been used as a well-known example of a breakthroughinthetargetedandlong-termdeliveryofmedications.ThreeARTdrugs(efavirenz, ritonavir, and lopinavir) were encapsulated as nanoparticles by the researchers utilizing PLGA. The nanoparticle approach provided a consistent release of drug for 4 weeksand beyond, while freemedicationsweregonein48hours.HIVinfectionandresidenceintheCNS,anotherlocation (HAND),resultinasevereneurocognitiveimpairmentthat isassociatedwithHIV. Additionally, nanoparticlesare known to beable to phagocytosetheir way beyondtheBBB.Studiesshowthat anti-HIV medications are successfully administered.

Themosteffectivewaytostopinfectionsis andtheonesforwhichimmunizationsarethegreatest treatments since they focus more on prevention than healing. A lot of work has gone into developing vaccines that block the viral agent effectively and efficiently. New methods are emerging that can be used to advance nanotechnology, such as genetic treatment and immunotherapy. Some nanoparticles themselves possess therapeutic properties.

Conclusion

AproblemforglobalpublichealthcontinuestobeHIV/AIDS.

Through this review, it is clear that the use of nanoparticles in HIV prevention and treatment has gained more traction recently.However, there are still barriers that need to be removed in order for NPs to reach their intended target sites, particularly in macrophages and brain tissues where antiretroviral drug penetration is less than ideal, leadingtoa slowandongoingintracellularreplicationofthevirallagent.DifferentNPs areutilisedtodeliverARTmedicationsbothwithinandoutsideofcells,andsomeNPs, includingfullerenes,inorganicnanoparticles,anddendrimers,have demonstratedanti- HIV efficacy outside of cells.

Withanumberofcutting-edgestrategies,nanotechnologyhasthepotentialto influence HIV/AIDS prevention and therapy. Using nanotechnology platforms for antiretroviral drug delivery may enhance treatment choices. The effectiveness of the treatment may rise as a result of better patient adherence to medication regimens brought on by controlled and prolonged drug release. Targeted nanoparticles have been utilised to attack macrophages, a significant HIV viral reservoir, using ligands such mannose, galactose, tufts in, and fMLF peptides. Targeted co-delivery of two or more antiviral medications in nanoparticle technology may significantly enhancetreatment of viral reservoirs in the future. Our team, together with other researchers, has created nanoparticles that may co-deliver hydrophobic and hydrophilic pharmaceuticals or genes,offeringadaptabilityfor theco-deliveryofantiviral medications.Nanomaterials havedemonstratedtheir capacitytopreventviralmultiplicationontheir own,inaddition to delivering antiviral medications. Dendrimers, gold nanoparticles, fullerenes, and inorganic nanoparticles like silver have antiviral properties or enhance the antiviral properties of other compounds.

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