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Delivery of Anti-Hiv Drugs of Targeting Strategies

Ankit Mishra*

Department of Psychology, University of Connecticut, United States

Corresponding author: Ankit Mishra

AnkitMishra76@gmail.com

Department of Psychology, University of Connecticut, United States

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Abstract

Infection with the human immunodeficiency virus continues to be a leading cause of death worldwide. The current antiretroviral therapy has a number of drawbacks, including toxicity, drug-drug interactions, the development of drug resistance, the need for long-term drug therapy, poor bioavailability, and lack of access to tissues and reservoirs, even though it has significantly decreased AIDS-related morbidity and mortality. Recent anti-HIV therapeutic research has concentrated on developing drug delivery methods that are selectively targeted to host cells that are HIV-infected or at risk of becoming HIV-positive in order to get around these issues. In this context, a number of surface molecules with both viral and host cell cellular origins have been identified in recent years, which might allow for the targeted administration of drugs to HIV-infected individuals. In this review, we give a thorough overview of the need. Identifying novel viral and host-cell molecules for novel drug delivery systems, as well as the accomplishments and difficulties in doing so for targeted drug delivery of anti-HIV medications. Such customised anti-retroviral drug delivery strategies may open the door to the successful management and elimination of HIV in humans.

Keywords: HIV; Aids; Targeted Drug delivery; Viral targets; Host targets

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Introduction

Acquired Immuno Deficiency Syndrome, a leading cause of mortality worldwide, is mostly brought on by the human immunodeficiency virus. HIV primarily targets CD4+ T cells, monocytes, macrophages, and dendritic cells in the immune system. The severe immune suppression that defines the advanced stage of AIDS is caused by a reduction in CD4+ T-cells in the more advanced stages of infection [1]. But the introduction of Highly Active Antiretroviral Therapy, a cocktail of medications that prevent HIV-1 replication, has lowered viremia, delayed the emergence of opportunistic infections in the majority of patients, and extended survival [2]. The primary method of treating AIDS has been chemotherapy [3]. The most prevalent drug classes used to treat HIV infections are meant to block a certain type of stage in the HIV infection cycle [4]. The numerous antiretroviral medicines' varied targets are shown in HIV cannot enter the host cell because of entrance inhibitors such fusion inhibitors and corrector inhibitors [5]. While corrector inhibitors bind with the CCR5 receptor in the host cell and prohibit interactions with the viral glycoprotein-120, fusion inhibitors interact with the viral glycoprotein-41 on the viral envelope, preventing its fusion with the cell membrane [6]. Through binding contacts with the HIV protease's active site, protease inhibitors prevent the proteolytic processing of viral proteins [7]. Inhibitors of reverse transcriptase make up a significant class of anti-retroviral medications. These molecules prevent the viral genome's single-stranded RNA from becoming a double-stranded one [8]. Nucleoside reverse transcriptase inhibitors and nucleotide reverse transcriptase inhibitors, respectively, are the terms used to describe these substances [9]. These inhibitors stop the HIV life cycle by attaching directly to the reverse transcriptase enzyme [10].

Discussion

Reverse transcriptase activity is inhibited by a related class of medications called non-nucleoside reverse transcriptase inhibitors, which attach to an allosteric location on the enzyme [11]. Integrase inhibitors, which prevent the integration of the viral genome with the host cell, are a recent addition to the

class of anti-retroviral medications [12]. There is a list of anti-HIV medications in Long-term uninterrupted multi-drug ARV therapy is required due to the nature of HIV infection, including viral persistence in reservoirs [13]. Whether a patient is treatment-experienced or treatment-naive, compliance with therapy is crucial since low patient compliance frequently contributes to treatment failure and viral rebound [14]. The cumulative expenditures of combination ARV therapy further worsen the lack of patient adherence to complex drug administration regimens [15]. Drug-drug interactions and toxicity Constipation, fever, liver problems, muscular dystrophy, metabolic problems, and peripheral neuropathy are just a few of the side effects that have been linked to prolonged ARV therapy. The efficacy of the pharmaceuticals can be decreased by unfavourable drug-drug interactions caused by the use of a combination of medications in traditional therapy. As an illustration, when the reverse transcriptase inhibitor Saquinavir levels in the plasma were observed to reduce quickly when nevirapine and the protease inhibitor saquinavir were used to treat HIV infections. This is because nevirapine induces the liver's cytochrome p450, which then metabolises and excretes saquinavir, decreasing both its availability and effectiveness. Poor pharmacokinetics: ARV medicines suffer from poor bioavailability. The majority of ARV medications are designed as solid dose forms for oral use. Although oral dosage forms are more convenient, the total dose of the chemicals in a typical therapeutic regimen is large. Because the treatment goal is to totally suppress viral growth, an effect that is proportional to medication concentrations, high doses are desired. The oral route for medication distribution suffers from a significant first-pass effect, gastrointestinal tract enzyme variations that affect absorption and breakdown, and high pH conditions that cause low and irregular bioavailability. For instance, their oral bioavailability is further reduced by the development of multidrug resistant efflux proteins like P-glycoprotein on the gastrointestinal tract. The amount of effective anti-HIV medication that reaches the target action site will be significantly decreased by the metabolism/elimination and transport obstacles. Many ARV medications have a short half-life, which necessitates frequent dose administration, which results in poor patient compliance. Due to the medication's short plasma half-life and short plasma residence time, frequent booster dose administration and higher drug dosages are required, which leads to the emergence of drug resistance.

Conclusion

Several anti-retroviral medications, such saquinavir have low bioavailability. Low-density lipoproteins are a particular class of lipoproteins that help carry fats into cells. LDL has been investigated as a potential targeting molecule against HIV-infected macrophages because of its capacity to attract macrophages. It has been proven that LDL conjugated AZT azido thymidine can be delivered to macrophages by LDL receptor-mediated endocytosis. Similar studies have been done with LDL conjugated fluorothymidine, which attaches to HIV-infected macrophages and effectively delivers the medication, resulting in a reduction in viral load as compared to the free drug. For site-specific delivery of AZT to macrophages, acetylated LDL loaded LDL was used in another investigation. Scavenger receptors enabled the absorption of acetylated LDL modified carriers, which decreased the viral Targeting the LDL receptor during the later stages of the disease, however, may not be a successful tactic due to the fact that it has been discovered that HIV infections cause a decrease in the expression of the LDL receptor. The internalisation of the carrier into the desired site is mostly influenced by unique characteristics of the targeted cells in passive targeting, which does not entail any chemical modification of the carrier. Utilizing the increased permeability and retention (EPR) feature of cancer cells, the notion of passive targeting has been successfully used to cancer therapies. HIV infections were discovered to be transmitted to CD4+ TH cells through virological synapses by dendritic cells and macrophages with high levels of viral particles. These dendritic cells and macrophages have been found to be quite active. During HIV infections, infected cells are more phagocytic than uninfected cells. It is possible to use the macrophages' increased phagocytic activity to capture anti-retroviral-loaded carriers in HIV-infected cells. Indinavir-encapsulated liposomal nanoparticles made with synthetic phospholipids phosphatide choline, phosphatidyl ethanolamine, and stabilising agents were used to successfully demonstrate this passive targeting technique. When compared to soluble indinavir, these nanoparticles considerably decreased the viral load and showed good absorption in HIV-infected macrophages. This distinction between the drug's encapsulated and free forms was mostly owing to macrophages' phagocytosis of the nanoparticles. Another method involved the synthesis of a self-assembled dual drug combination of didanosine and AZT zidovudine separated by an adeoxycholyl spacer. This didanosine-deoxycholllyl-phosphoryl zidovudine the phagocytic macrophages readily absorbed conjugate, which led to the virions being destroyed. The schematic depicts the internalisation of nanoparticles by infected cells following passive targeting. In order to combat the development of medication resistance and many negative consequences associated with long-term ARV therapy use, it is still imperative that novel medicines be developed. Numerous ARV medications also have short half-lives, necessitating frequent dose administration, which in turn results in poor patient compliance. Therefore, a natural strategy to get around these issues and effectively treat HIV infection is to use innovative medication delivery systems. Among the most recent therapeutic strategies, creating efficient drug delivery systems for the tried-and-true medications is a top priority. The necessity of novel drug delivery methods, benefits, and recent advances in the identification of viral and host surface molecules as markers for targeted drug delivery of antiretroviral medications were covered in this review. These results provide new opportunities for in-depth research on the efficiency of these targeting techniques in HIV therapy. Such a thorough strategy might finally prove successful in eradicating virus from reservoirs as well as lowering viral load.

Acknowledgement

None

Conflict of Interest

No conflict of interest

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