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Nano Particle-Based Drug For Treatment Of Covid-19

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1. Introduction

The coronavirus disease 2019 (COVID-19) outbreak has been caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV2, are single-stranded enveloped viruses belonging to the order Nidovirales and family Coronaviridae. It is a type of betacoronavirus that structurally contain four main proteins: the spike (S) glycoprotein, a small envelope (E) glycoprotein, a membrane (M) glycoprotein, and a nucleocapsid (N) protein (1). The SARS-CoV2 affects primarily the respiratory system of the humans where the S protein targets the cell surface receptor, angiotensin-converting enzyme II (ACEII) for its uptake and entry into the host cells. The binding of the S spike protein of the virus with ACEII is a primary criterion for the infection (2). With an ever increasing number of cases, various modes of treatment have been studied but none have proved to be completely effective in combating the coronavirus primarily on account of the emergence of new viral strains that has developed due to the repeated mutations that the virus has been undergoing.

The first therapeutic approaches in the treatment of COVID-19 were made by repurposing the well-known antiviral or antimicrobial agents along with interferons. The potential antiviral targets were initially pointed out by studying the viral replicative properties and the pathogenesis of the virus. These have helped in the use of drugs that have known pharmacokinetic profiles and are safe in the treatment of COVID-19 patients. Nucleoside analogs like Remdesivir (adenosine analog) (3-8), favipiravir, ribavirin (guanine analogs) (8-10); protease inhibitors lopinavir, ritonavir have been tested for inhibiting viral replication process at various stages (11-13). Chloroquine, the anti-malarial drug had also gained attention in the treatment of COVID-19, but like the other drugs, it has also proved to be ineffective and hence have not been considered for further use (8, 14-20).

Nanomedicine has been proved to be effective in combating various well-known diseases like HIV1 (21,22), Hepatitis-B Virus (23), influenza virus (24) and respiratory syncytial virus (25). As the traditional methods of therapeutic approaches in treatment of COVID-19 has remained away from success, researchers have moved their attention to the use of nanotechnology alone

and/or along with the combination of traditional methods for combating coronavirus. The applications of this new age technology in the field of medical sciences are commonly known as nanomedicines which uses nanoparticles for their unique properties. The nanoparticles help in the development of a more targeted, tissue specific, safer and personalized medical approach (26, 27) which can even cross biological barriers (28) in treating a disease besides their diagnosis and/or prevention. In the present pandemic situation these nanoparticles can not only help in development of new drugs with increased tissue specificity and activity, sustained release and reduced toxicity; but they might also provide a nano-based vaccination against coronavirus, augmenting the humoral as well as cellular immune responses.

The primary target of the coronavirus is the respiratory tract, specifically the ACEII receptors. Hence this is often taken as a first site for therapeutic approaches for the treatment of covid-19. With this view in mind, nanomedicine has been used in targeting the lungs through aerosol suspended nanoparticles for delivering drugs, mRNAs and therapeutic proteins (29, 30). The first approach might be to introduce an "entry inhibitor" which can block the interaction of the virus with the cells (31, 32). A nanoparticle entry inhibitor blocking the interaction of spike S protein with cellular ACE2 receptor could do the trick (33-36). Development of various nanoparticles like polymers to oligomers and liposomes (37-39) which could act as an entry inhibitors by binding to the virus, damaging it and rendering it irreversibly ineffective might be a good antiviral approach of nanomedicine (40) in combating coronavirus infections.

The second and most sought after approach for a broader and more efficient control of the virus is the development of a nanoparticle-based vaccine that would not only target the virus but would also help in modulation of the immune responses of the host to the viral particles (41). The efficient targeting of the viral spike proteins by antigens requires a suitable carrier to avoid cargo degradation, enhance bioavailability and clearance. Nanocarriers being biocompatible could be easily used for encapsulation of cargo with high loading efficiency (29). These carriers are also used for delivery of mRNAs or siRNAs enabling synthesis of key viral proteins, inactivating critical viral target genes, etc (30).

Live attenuated viruses being highly immunogenic, initial extensive safety tests must be done to ensure their usage. However, inactivated vaccines and recombinant-protein vaccines are safe but need the presence of adjuvants to enhance their immunogenicity. In covid-19 besides enhancing the effectivity of such vaccines, adjuvants would also reduce the dosage of the vaccine protein required per unit (nn3697). Several materials at a nano quantity could work as a suitable adjuvant in combination with vaccines. Besides being adjuvants several nanoparticles like graphene, carbon nanotubes, polystyrene particles, nanodiamonds also function as immune modulators either activating or suppressing the immune responses (42-45) by activating STAT1/IRF1 interferon signalling in monocytes and T cells, producing T cell chemoattractants and macrophage1/T helper1 polarization of immune response (44). As COVID-19 often causes ARDS (acute respiratory distress syndrome) by triggering the cytokine storm (46), the nanoparticles may be used in not only modulation of the immune response but also in targeted delivery of immunosuppressants and receptor blockers for IL-6, one of the key players of cytokine storm (47). The use of nanoparticles that have been octadecylamine-functionalised and dexamethasone-adsorbed for anti-inflammatory and proregenerative purposes have also been explored (48).

Besides the conventional therapeutic approaches, nanoparticles in the form of carbon quantum dots (CQDs) may be used for inhibition of early stage interaction of the viral S protein with the host cells (49). Similarly biomimetic nanodecoys like reconstituted lipoproteins, liposomal formulations and cell-membrane nanostructures may be used lure viruses (50, 51).

2. Conclusion

It may be concluded from the evidences that the applications of nanomedicine in the treatment and prevention of COVID-19 are promising. However, the utility faces key challenges not only in understanding the viral genomics and pathogenesis but also in the development of a safe nanoparticle-based procedure that may help answer the therapeutic necessity of the COVID-19 patients.

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