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Bite-sized Review on Advance Delivery System, Support in the management of Covid-19

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Abstract

COVID-19 are an unprecedented challenge for healthcare providers; there are no approved treatments for this disease, nor are there no approved vaccines. The sources of infection of novel coronavirus detected mainly from animals to humans or infected human to healthy human through respiratory droplets and long contact period are the most prominent way of transmission. The capability of regular therapies is constantly fading away exactly in case of coronavirus due to the modification of new strain, which could be certainly due to speedy adaptation in a protein sequence. The scientist should understand the pandemic situation of virus infection, also as they ought to identify the newest pathway research to regulate the virus infection. Developing new and smart strategies for drugs already in the development pipeline or already exiting drug can be treating diseases in patients could be useful to fight against COVID-19. In the last few years, several new smart drug delivery approaches made the changeover from the laboratory development to clinical applications. At present technology, researchers provide effective and low toxicity drug delivery when compared with classical delivery. This approach will be a great opportunity for the scientist to work and update preclinical research of advance drug delivery systems to clone able and convertible production to the human trial success rate. By understanding the new drug delivery research approaches for antiviral therapy are increases to produce safe and high-quality therapies at reasonable costs.

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INTRODUCTION

COVID-19 are an unprecedented challenge for healthcare providers; there are no approved treatments for this disease, nor are there no approved vaccines. The viral infection first identified in enormous sort of animal-like perhaps bats that spread to other animals like civet cats, which named as a severe acute respiratory syndrome, called SARS, which appeared in 2002–2003 as a coronavirus from southern China and circulated throughout the universe (Calisher *et al.*, 2006). SARS infection was

reported in 29 countries such as North America, South America, Europe, Asia etc. In animal, the viruses RNA sequence sustained the integrity of the tenth open reading frame whereas, within the human, the virus sequence results in two overlapping open reading frame (Dominguez *et al.*, 2009). The function of the open reading frame in the animal and human isolates is unknown, the deletion of the 29-nucleotide sequence played a major role in the transspecies skip, it could lead to modification of the strain. The current outbreak of novel coronavirus was first reported on Dec 31, 2019, from Wuhan, China. It was named as 2019-nCoV by World Health Organization on Jan 12 (World Health Organization (WHO), 2020). Novel beta coronavirus, which belongs to the SARS virus subgroup of the Coronaviridae family. WHO Director-General has declared the covid is a pandemic situation. February 6, 2020, nCoV has infected human and 564 deaths reported everywhere the world (Lam *et al.*, 2003). The sources of infection novel coronavirus detected mainly from animals to humans or infected human to healthy human through respiratory droplets and long contact period are the most prominent way of transmission (Consensus, 2020). So, the disease burdens are increasing across the world, to encounter the disease researchers are providing the advanced novel drug delivery systems for maintenance of bioavailability of drug as per patient need, also because of the rate of drug delivery (Wen *et al.*, 2015). That developing new and smart delivery strategies of drugs already in the development pipeline or already exiting drug can be treating diseases in patients could be useful to fight against COVID-19. The advance drug delivery technology will be a bridge for developing a drug therapy to kill or manage Covid-19 Infection.

Newly Identified Group I & Group II Corono Viruses

The field of corona virology has advancement in recent days to identify the strain of the virus. Severe Acute Respiratory Syndrome epidemic was a stunning mark, that animal coronaviruses are dangerous threats to the humans (Kahn and McIntosh, 2005). The precise reason behind spreading the virus from species to species remains obscure. NL63 virus has been identified in many countries, this sort of virus and therefore the similar viruses HCoV-NH and NL are likely the reason behind a considerable proportion of respiratory tract disease in infants and youngsters (Esper *et al.*, 2005). It has been clarified that the coronaviruses infect humans and causes associated respiratory problems and widely distributed among groups I and II species.

In 2004, new human coronavirus was documented, NL63, isolated from a 7-month-old girl with coryza, conjunctivitis, fever, and bronchiolitis. Introducing a unique genomic amplification technique were able to sequence the whole viral genome. By this technique, Coronavirus entire genomic sequence was analysed that result shows the virus also belonged to group I coronavirus and closely associated with NL63. Sequence and phylogenetic analysis supported the replicase gene showed that HCoV-NH was closely associated with both NL63 and NL. (Pyrc *et al.*, 2007). Similarly, group I virus's species are closely related and which represent the identical viral species (Esper *et al.*, 2006).

In January 2001, a 71-year-old man who had recently returned from Shenzhen, China, a previously SARS-endemic area, presented in Hong Kong with a fever and productive cough. Severe Acute Respiratory Syndrome screening was negative, and a unique group II coronavirus sequence was amplified by RT-PCR from his respiratory specimen with the use of primers that targeted conserved regions of the viral replicase gene (Esper *et al.*, 2006). This novel virus, designated HKU1, was genetically distinct from OC43, the other known human group II coronavirus. This virus couldn't be propagated in cell culture. Seroepidemiologic studies, supported antibodies reacting with a recombinant HKU1 nucleocapsid, suggested that human affected with HKU1 could be common (Esper *et al.*, 2006).

Corono Virus Genome and Structure

Coronaviruses are structurally large-sized single-stranded RNA viruses, in which nucleic acid is about 30 kb long (Consensus, 2020). The surface polyproteins are covered by viral-encoded proteases to form the entire capsid. An RNA polymerase and an ATPase helicase; surface hemagglutinin-esterase protein are present; the broad surface glycoprotein (S protein) that forms the petal-shaped surface projections; a small envelope protein (E protein); a membrane glycoprotein (M protein); and a nucleocapsid protein (N protein) that forms a complex with the RNA to form the capsid (Li, 2016). coronaviruses are capable of infecting the human cell very easily.

Recent Treatment

Present-day, there's no targeted antiviral therapy or vaccine for 2019-nCoV infection. Because of ongoing studies, the scientist should concentrate on the danger of usage of medicine under special circumstances, also as they ought to identify the newest pathway research to regulate the virus (Consensus, 2020). The subsequent drugs could also be utilized in clinical practice and clinical trials.

Supportive Treatment

Nonsteroidal anti-inflammatory drugs, antitussive, Interferon, Lopinavir/ritonavir, Ribavirin, Antimicrobial agents, hydroxychloroquine, Corticosteroids, intestinal microecological preparations could be used for supportive treatment.

Nutrition Support Therapy

For patients with severe gastrointestinal dysfunction, other complications with drug or disease, nutrition supplements are required to satisfy the essential nutritional needs. Within the early stages, the permissive low-calories are required to reach 60% to 80% of the nutritional intake. When the disease was elevated, energy and nutrients are required more to keep up the nutritional level within the body.

Traditional Medicine Treatment

The diseases are often treated by traditional natural medicine pestilence. Based on the development of the illness, respiratory associated disease, and other complication, the following treatment options can be selected for syndrome differentiation and treatment (Consensus, 2020).

1. Jinhua Qinggan Granule: Dispelling wind to ventilate the lungs, clearing heat and detoxifying.
2. LianhuaQingwen Capsule (in granules): Heat-clearing and detoxifying, removing lung hotness.
3. Shengmai injection: Recovering pulses for resuscitation, Qi-boosting and Yin nurturing.
4. Xuebijing Injection: Dissolving blood stasis and detoxifying.
5. Shenfu injection: Reviving yang for resuscitation, Qi-boosting, and exterior-securing.

Food Interactions with Medicines

Use of tobacco alcohol, spicy food, and seafood should be avoided while taking with drugs. Medicines like antipyretic and detoxicate effects should not be used with nourishing traditional medicines concurrently.

Adverse Drug Reactions

Pharmacists should pay attention to the adverse reactions, especially those who are still being assessed and under clinical trials. Identify the causal relationship between adverse drug reactions and symptoms of nCoV infection (Chilvers *et al.*, 2001). Proper monitoring and surveillance needed for repurposing drugs and new drugs in clinical trials to make sure the safety of the clinical medication.

Drug Delivery Systems

Morden approaches of drug delivery systems are used to target the specific drug release modification system, which helps to enhance health and extend lives. This system has modified excellently within the few decades and even larger changes are anticipated within close to the future (Zhou *et al.*, 2015). By acknowledging the physical barriers, this could improve delivery system, like movement in the vascular system and drug transfer through cells and tissues; they need to commit to developing many new mechanisms of drug delivery that have entered clinical apply. With all of this progress, several drugs, even those developed using the advanced biological methods, have unacceptable adverse effects because of the medicine interacting with healthy tissues. These side effects restrain our potency from designing best optimal medications for several conditions like cancer, Alzheimer's disease and infectious diseases. Based on the therapy, the way it is delivered, and how our bodies respond, adverse effects are some of the important key points for the designing delivery system (Ud *et al.*, 2017). These adverse reactions can greatly vary from induvial to induvial. Based on advance drug delivery system side effect of an individual person can be minimized.

Delivery Systems used in Current Medical Practice

In the last few years, many new advanced drug delivery systems have made the transition from the laboratory to clinical practise (Brouwers, 1996) and advanced delivery systems at existing medical practices which proved useful or have reduced toxicity compared with classical dosage forms.

1. Novel macromolecular and supra-molecular materials for drug delivery.

e.g., biodegradable polymers, hydrogels, poly methyl methacrylate

2. Innovative drug delivery systems:

e.g., liposomes, transdermal systems, micelle systems, improved systems for oral delivery, external- and implantable pumps.

3. New therapeutic approaches based on advanced drug delivery.

e.g., Gene therapy, and infections, cell drug delivery, chemotherapy, peptide and protein delivery coating on implantable.

Routes of Delivery

The drug can be administered in several ways by swallowing, inhalation, absorption through the skin,

or injection delivery. Each technique has its own benefits and risk; regular strategies of delivery cannot be followed for each therapy. Developing an advance delivery approaches or designing a new delivery which can enhance the use of existing conversional delivery (Kerry *et al.*, 2019). Moreover, these application in biomedical science are still lurking and should be prioritized to bridge the gap (Kerry *et al.*, 2019). The potency of conventional therapies is gradually disappearing away specifically in case of viral infections due to the development of resistance against the specific drug, which could be certainly due to accelerated adaptation in peripheral protein sequence leading to new-fangled viral strain.

Nanotechnology

Nanotechnology is the new avenues for exposing drug delivery. The nanoparticles target the precise area by delivering efficient medicine and kill the infected cell (Patra *et al.*, 2018). The Researchers have reported promising leads to develop a treatment for nanoparticle method replaces this sort to kill viruses, which might have unpredictable outcomes.

Nano-Based Approach of Therapy for Inhibit nCOVID-19

Nano based therapy primarily inhibit or inactivate the virus virulence. Nano-based antiviral agents are generally classified based on extending from basic inorganic nanoparticles to complex organic particles and hybrid nanosystems (Singh and Lillard, 2009). Metallic Nanoparticles and nanocarriers are designed in the form of nanospheres, nanocapsule, and nanocage could be categorized under inorganic nanoparticles. In Organic nanoparticles, encapsulation drugs reduce the toxicity of the target drug. The mechanism of drug delivery could be modified by developing a specific target design. But. Only certain specific organic nanoparticles are presently being evaluated for their antiviral therapy. These include polymeric of Nanoparticles, lipid nanoparticles, neosomes, and nano-micelles can be used against different virus strain.

Gold Nanoparticles

Gold nanoparticles are an effective method of delivery which are directly used as an antiviral agent. Ongoing research on gold nanoparticles upholds with some biocompatible polymer which acts as an effective antiviral agent for infecting virus. The scientist had speculated that the mechanism of antiviral activity of polyethylene glycol encapsulated gold nanoparticles against HIV, blocking the glycol protein 120 by attachment with CD4, which results in inhibit viral entry. Scientists are started to involve in the later research on which AuNPs have arrested FMDV replication at the pre-entry stage, associated specifically with transcription within the host cell.

Silica Nanocarriers

Silica Nanoparticles have some unique characteristics like tuneable diameter, pore size, convenience in functionalization, biocompatibilities, etc., are well appreciated for research all over the world. Apart from these, there are two other important properties, such as self- immobilization of ligands onto the surface of Silica Nanoparticles and stimuli-responsive gatekeepers (Phillips *et al.*, 2010). Recently, photodynamic therapy by functionalizing Silica Nanoparticles with photosensitizers is one of the fastest emerging research (Kerry *et al.*, 2019). At present, the antiviral activity of Silica Nanoparticles against some viruses like Human and animal causing virus has been demonstrated and reported. And the mode of antiviral activity is either mediated by immunization of the host against virus or by inhibiting viral entry.

Polymeric Nanoparticles

The utilization of polymeric Nanoparticles for the development of effective antiviral therapy has been occurring form past few decades. Many different natures of polymers such as synthetic and natural have immensely contributed to the meticulous understanding of ideal properties such as bioavailability, biocompatibility, immune compatibility, etc. But, the polymeric nanoparticles are uses for the development of an antiviral therapy which have been researched only for few specific viruses such as influenza, HIV and rabies virus (Kerry *et al.*, 2019). The polymeric Nanoparticles in the near future are certainly going to be soon used for the development of a novel antiviral against a divergent array of infectious viruses.

Lipid-Based Nanoparticles

This drug delivery systems are widely used in research work for its own advantage. Developing nanostructured lipid carriers or solid-lipid Nanoparticles were showing better ability as an exceptionally feasible biocompatible material for therapeutics development in the field of advanced medicine. Ongoing researches of lipid-based Nanomaterials has exploitation to develop a unique antiviral agent against the specific virus (García-Pinel *et al.*, 2019). The recent enquiry these nano lipid applications are used to develop antiviral against for some viruses like Hepatitis C virus and HIV has been reported. In forthcoming years, this type of drug delivery system will provide a great

opportunity to design drug molecules against a different strain of the virus.

Chitosan DNA Nano Complex

Chitosan can react ionically with the anion charged DNA and forms nanocomplexes (Cao *et al.*, 2019). This nano complexes DNA act better protected against nuclease degradation, which shows promising efficiency. Based on the charges present in the virus shell, this approach can be used to make an easy complex with virus shell and inactivate perfectly. (Raftery *et al.*, 2013).

Plant Virus Nanoparticle

Reverse engineering technology is a promising way to solve some issue. Based on this approach, scientist designed a plant virus nanoparticle that can target and attach to infected cells (Shoeb and Hefferon, 2019) or attack, fight against other viruses. Viral based nanoparticles take its own benefit of the natural ways to develop past immune defences by which viral nanoparticles are designed similar structure of the regular infected virus, and they do not require any alteration as much as other types of conventional nanoparticles. Plant-based viral nanoparticles are generally biodegradable in nature, which is harmless to humans begins.

Advance Research in Drug Delivery Systems

Researchers understood the diseases progress & development strategies of the virus inside the host cell; they're also acquiring more knowledge about the various response developed in human bodies against the virus illness. Including advances technology, unique strategies for drug delivery science may help to deliver the medicine against virus and minimize the associate illness.

Nanomedicine for Advanced Drug Delivery

Nanomedicine is the fast-growing area that's revolutionizing for a specific infection (Senapati *et al.*, 2018). Nanomedicine has unique properties such as tiny size (diameter within 1–100 nm), which help to bind, absorb and carry agents, for drugs, DNA, RNA, and proteins.

1. Organic Nano carriers hold liposomes, lipids, dendrimers, carbon nanotubes, emulsions, and synthetic polymers.
2. Inorganic Nano carrier is the intensively investigated for medicine, which is delivered through Quantum dots, carbon nanotubes, layered double hydroxides, mesoporous silica, and magnetic nanoparticles technology.

Carbon-Based Nanocarriers

This is the most recent technology of nanoparticulated systems in biotherapeutic applications. These nanomaterials such as carbon nanotubes, fullerenes, nano-horns, nanodots and nanodiamonds etc., Carbon-based nanomaterials have spectacular beneficiary properties, in spite, their utilization in the field of virology is restricted to some viruses (Maiti *et al.*, 2018). But scientist, undergoing research on antiviral activities based on carbon nanomaterials against viruses like Ebola virus and Respiratory syncytial virus.

Quantum Dots

Quantum dots are tiny semiconductor particles they have been developed as a new type of fluorescent labels designed for the field biology and medicine. Along with a single excitation source, the multicolour imaging can be achieved probably by the QDs with their specific features like Narrow emission and broad absorption. (Granada *et al.*, 2018) The common metal composition of quantum dots includes zinc, lead, mercury and cadmium. Scientific research shows that fluorescent quantum rods are one of the forms of quantum dots in coupling to targeting materials and Highly active antiretroviral therapy—Nano delivery of drugs with quantum dots, which shows hopeful antiviral agent against HIV. Green fluorescence bio dye coated with quantum dots are designed to have a high affinity towards the target virus capsid, passing external light source quantum dots coated fluorescence emits the radiation which destroys the virus capsid.

Nano Vaccine

Inclusion to drugs and novel vaccines, scientist are approaching to enhance the immune response against infectious disease by using nano vaccines for the specific virus strain (Vijayan *et al.*, 2019). Scientist extended the life of mice with skin cancer by treating with nano vaccine, which forms a complex with bacterial DNA to activate a specific immune response, which shoes promising result that the nano vaccine remains longer in the targeting environment and trigging the immune cells to recognize targeting cells as foreign bodies and attack them (Luo *et al.*, 2017). The same strategy of the delivery system can be incorporated into ncovid-19 infection to retain a long time and develop an immune response against ncovid.

Endosomal pH

Endosomal pH approach is the unique strategies by which the virus entered into the host cell; the subsequent life cycle of SERS-CoV requires low pH. Inhibitors of pH-sensitive endosomal protease block CoV infection. Several different small compounds

and molecules have been reported against virus infection. Vacuoles on exposure to drugs show alteration in intracellular organelles especially enlargement of late endosomes. In *an in-vitro* environment, the drug inhibited coronavirus infection in Vero cells (46).

Osmotic Shock and the Viral Strength of Capsid

Osmotic shock approaches are the domestic means for breaking viral capsids and leakage of their genomic materials. At suitable conditions, providing high-concentration of salt solutions which will slowly permeable to the capsids through salt ions exchanger, (Choi *et al.*, 2015). By this exchange internal osmotic pressure of viral capsid will be increased which lead to busting or leaking of the capsid. Osmotic leakage properties of the inactivated influenza virus were analysed by SFLS (Cordova *et al.*, 2003). The osmotic performance of the virus was determined by recording the beam of light scattering after a fast mixing of effective influenza virus (Normal saline) and inactive (concentrated Nacl) influenza virus.

Monoclonal Antibodies Therapy

Monoclonal antibodies approaches are advance therapy against viral infection. Targeting specific Proteins in viral capsid surface like F-protein, G-protein or M proteins and producing its action. Further several broad-spectrum antiviral agents like ribavirin, remdesivir, balapiravir and most current drug favipiravir are the inhibitor of viral RNA (Agostini *et al.*, 2018). But there is a lack of research on target delivery of monoclonal antibodies and cell toxicity against new strain virus (Roberts *et al.*, 2006). Due to the severity of the infection, a scientist needs to pay attention to the monoclonal antibody approach to design the specific target delivery, which attacks the capsid protein directly and give better action against covid-19.

CONCLUSION

Currently, there's no specific antiviral treatment or vaccine for 2019-nCoV infection. A scientist needs to develop the advance drug delivery approach by applying new strategies for attacking viral disease. Based on the forecast, in the future antiviral research will be the most leading research in the world for developing an easy delivery system to kill the virus without any cytotoxicity and with high biocompatibility. This approach will be a great opportunity for the scientist to work and update preclinical research of advance drug delivery systems to cloneable and convertible production to the human trial success rate. In conclusion, the advance and smart delivery system which help to bind, absorb, carrying materials, for drugs, DNA, RNA, and proteins, together with imaging agents which produce more efficiency towards nCvid-19 by produce safe and high-quality treatment at reasonable costs.

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Conflict of Interest

The authors declare that they do not have any conflict of interest.

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