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RESEARCH ARTICLE

ROLE OF NANOTECHNOLOGY IN CURRENT ADVANCEMENT VACCINE DEVELOPMENT FOR COVID-19

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Abstract: The most recent human coronavirus known as COVID-19(SARS-CoV-2) has already spread around the world. This review describes the accumulated knowledge of the previous SARS-CoV, MERS-CoV infections and aim to help understand the newly emerged SARS-CoV-2 infection. Advances in nanotechnology over the past decades to develop new nanomaterials and step forward in the application of new technology tools. Finally nanotechnology approach describes vaccine development and therapeutics drugs developed nanomedicines which are currently undergoing clinical trial to become innovative alternatives for overcoming COVID-19 vaccine. Nanoparticles are non-toxic antiviral showed great promise to provide nano vaccine against viral infection.

Keywords: Nanotechnology, Vaccine Development, COVID-19.

INTRODUCTION

COVID-19 is caused by SARS-CoV-2 Virus and it has recently become one of the most challenging pandemics of the last century. Corona virus encodes some structural and non-structural protein that might be considered as an antiviral target, including phosphorylated nucleocapsid envelop, membrane glycoprotein, spike helicase, papain like protease and chymotrypsin like protease. Both severe acute respiratory syndrome (SARS) and (MERS) middle east respiratory syndrome are started in late 2012.Coronavirus is responsible for both SARS and COVID-19 attached to the receptor binding site of angiotensin-converting enzyme2 (ACE2). MERS was started from Soudiarabia with animal sources of camel &dipeptidyl peptidase-4 receptor involvement. Pathologically ACE-2 a cell surface receptor in human the receptor of the SARS-CoV-2virus.CD147 as an extracellular matrix metalloprotease inducer is considered as the other receptor for SARS-CoV-2 on the surface of lots cells including end of helical cell, epithelial cell and endothelial cell. Alpha, Beta, gamma and delta are four classes of the corona virus (CoV) family all featuring a single stranded positive sense RNA genome. The membrane envelops encapsulated the viral genome are decorated with glycoprotein spike transmembrane protein. The word corona viruses named for the club shaped protein spikes on their surface when viewed under transmission electron microscope. The causative agents for COVID-19 are beta cells [1]. Furthermore nanotechnology tools can provide a broader overview of the new vaccine design strategies. Nano based formulations for SARS-CoV-2 Therapeutics is being developed as aa delivering vehicle along with a novel nano-vaccine metastasis form and useful nano drugs for treating SARS-CoV-2 infection. The spike (S) protein is peplomers which is located outside the lipid envelope and the ss protein is highly amino acids sequence. The spike protein is directly interacting with hosts cellular receptor and ACE-2 Angiotensinogen Converting Enzyme-2. After binding 'S' protein to ACE-2 Transmembrane Protease Serine-2 and furine in the host cell membrane simultaneously cleaves the 'S' protein to activate SARA-CoV-2.Then only SARS-CoV-2 is spread by direct contact with mucos membrane. In

the experiment using Vero cells. Plasmid based SiRNAs designed especially for the viral RNA polymerase have been shown to inhibit the SARS-CoV-2 to cytopathic effect [2].

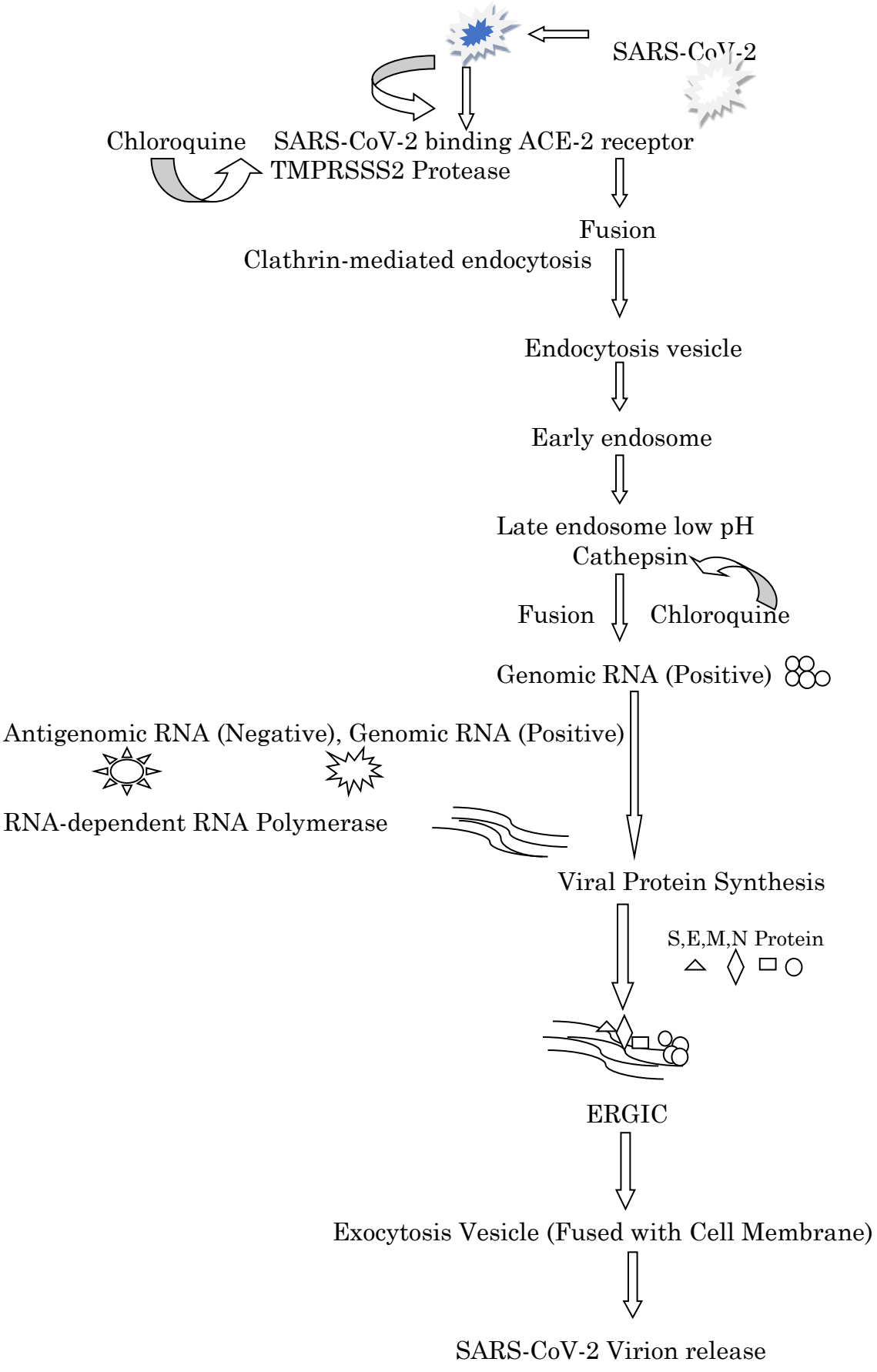

Fig.1: Schematic representation of the life cycle of SARS-CoV-2

Schematic diagram represent that SARS-CoV-2 binds to Angiotensinogen Converting Enzyme-2 receptor using 'S' protein and undergoes cleavage by TMPRSS2 protease then inhibition of antibody neutralisation. Further spike protein cleave by cathepsin L resulting fusion of endosomal membrane with viral envelope to lead release of viral genome to cell cytoplasm ,after that transcription, translation of positive RNA and protein. Chloroquine influence the life cycle of SARS-Cov-2 through glycosylation of ACE2 receptor. At last final virion released from host cell.

- Cell Surface Receptor Binding
- Endocytosis of Viral Particle
- Virus Transport
- Virus Uncoating
- Transcription
- Translation
- Post-Translational Modification of Viral Proteins
- Assembly
- Budding

RNA interference (RNAi) demonstrated supress the expression of spike protein and nucleocapsid protein. When RNAi is applied to SARS-CoV infected cells, In primate cell SiRNA duplexes targeting SARS-CoV genomic RNA have been proposed as a new therapeutics strategy for SARS-CoV because it can degrade specific mRNAs, inhibition of SARS-CoV by RNAi in cultured cells and animal tissue have been reported.

Currently in order to overcome some deficiency pertaining to the aging immune system .Co-administered of adjuvant or cytokines that completely Activate Antigen Presenting Cell (APC). If a basic strategy aimed at developing vaccines for the elderly continually developed it will make a significant contribution to the research one effective SARS-CoV-2.

This is similar to SARS-CoV-2 and its infections not limited to any particular and people of all groups are vulnerable .SARS-CoV-2 belongs to beta coronavirus is identical genome sequence of SARS-CoV. When infected with SARS-CoV-2, macrophages , monocytes move to the site of infection T and B cell together induce an immune response 3,4].

This review introduce the main aspects as the structural characteristic of the virus, infection mechanism also presented a discussion about how nanotechnology can be applied in vaccine research and advantages over the conventional strategies.

Nano Technology-Based Vaccine Development

Recently nanoparticles as a promising approach to the development of new generation of vaccines. Nanoparticles can act both antigen and adjuvant. Nanoparticles are able to interact with cellular and humoral immunological responses.

It protect antigen against premature degradation and provide sustained release, enhanced antigen stability, reach targeted delivery of immunogen as well as increase the period of antigen exposure and uptake by Antigen Presenting Cells (APC). The fact that these systems can be delivered to cross cell membranes and target specific subcellular location enhances the potential of nano-based vaccine.

Different nanocarriers are lipid, polymer and polysaccharides and lipidic nanoparticles for the encapsulated of genetic material enhance immune response to the vaccine. Apart from that protect the DNA and RNA against enzymatic degradation and increase cell uptake, releasing the genetic materials in target cells. Antigen is encapsulated present inside the nanocarriers to the surface of the nanoparticles and administered together with the adjuvant to the target.

The efficacy of vaccines may be further enhanced through targeted modification to the nanoparticles antigen conjugates to achieve the desired level of immunological response. According to physical properties size, shape and surface charge of the nanoparticles can be functionalisation of the surface with a variety of ligands to make them adaptable vehicles for vaccine.

This can be administered via subcutaneous and intramuscular injection or by oral or intra nasal mucos as well as capillary penetration. RNA based vaccine working introducing a mRNA encoding a disease specific antigen.

Once sequence is create inside the cells, it serves as a template to produce the antigen in situ method. After translation process antigen extracellularly transported and recognised by antibodies or intracellularly processed presented to T-cell resulting in the humoral &cellular immune response. Vaccine for covid-19 were developed after publication of the complete genome of SARS-COV-2.

According to the WHO report upto 9 june 2020,B6 vaccine is being developed out of 10 which are currently on clinical trial phase.16 are nano based vaccine of covid-19.Co-interaction between nanoparticles and immune system produce better safety, quicker delivery and most effective vaccine compared to those developed by conventional therapy [5].

Subunit Vaccines

Spike protein is the most important for vaccine because membrane fusion and receptor binding sites are present on the s protein.

So that it inhibit viral infection by activating antibodies that prevent viral binding and sub sequent membrane fusion subunit vaccine enhance immunogenicity effectively by eliciting the immune response. RBD-based vaccines are effectively in preventive and therapeutic strategies and currently developed by man y research institute and multinational pharma companies [6].

Nucleic Acid Vaccine

Nucleic acid only structure also prevents the production of misfolded proteins that can occur in recombinant vaccine. The immunogenicity effect nucleic acid vaccine is influenced when plasmid injected into the cell and appropriate administered interval and route based on the principle nucleic acid vaccination is not effective immunisation method that was synthesized nucleic acid to elicit an immune response to produce live-attenuated nucleic acid vaccine does not require viruses, unlike conventional vaccine made of small subunit of inactivated or live pathogens.

Similar to RNA vaccine isa nucleic acid vaccine that can induce an immune response by being translated into protein within human cellS. mRNA vaccine not only lipid nanoparticles but also dendrimer nanoparticles and polymer nanoparticle are being used for effective delivery and high stability [7].

Nano Particle (NP): Based Vaccine

SARS-CoV, MERS-CoV has been utilised multiple times to introduce nanotechnology into vaccine or therapeutic research. Therefore the synthesized complex recognised by the T cell receptor increase the vaccine immunogenicity and efficiency, ensuring patient safety. Nanosized VLP entering to the host cell are directing involved in B cell activation and boosting the immune response.

MERS-CoV protein has been synthesized using the recombinant s protein in tested in animal model and linked to having increased immunogenicity. Nano sized virus like protein (VLPs) has a wide range of application enhances and effectiveness vaccine safety [8].

Research and development using innovative method such as nanotechnology is essential to end this pandemic effectively inherent time. Virus treatment using nano technology have been developed and commercialised for common virus infection such as IAV, IBV, EVB, HIV1, HSV1, HBV, HCV and HuNOV. The accumulated advancement in these virus fighting nanotechnologies can play important role in taking sars-Cov-2 treatment and vaccine development by Pfizer can be considered as great achievement of nanotechnology.

More ever this technology that derivatives SARS-CoV-2 in the eternal environment using nanomaterials such as Ag-NPs, NPs with Cu or CuO[314] and GD[316] and diagnostic nanotechnology that can quickly delete SARS-CoV-2 without use of expensive equipment by applying GNs, are also contributing towards the prevention & control of covid-19 [9].

Vaccine Development

Vaccine having two key components one is antigen which is the largest of the immune response and an adjuvant which is co-administered substances responsible for modulating the immune response against the antigen. Different generation of vaccine formulation controlled the spread of contagious disease used to elicit immune response.

First generation is attenuated or inactivated whole pathogen. This generation useful to prevent or control humans and animal. Second generation is recombinant subunit vaccine. This generation based upon non-pathogenic resources including synthetic peptide inactivated tins or recombinant protein vaccine.

Third vaccine is DNA and RNA Vaccine. Prime limitation is that falling to reach the target sites and necessity of boost the vaccination scheme with other immunogen agents as well as premature degradation of the antigen. So result is that weak immune response that's why it is not available in the market [10].

Table 1: Nano-based vaccine to prevent to prevent COVID-19

Name	Developer	Method	Development Phase
Ad5-nCoV (Adenovirus-5)	Cansino	Ad-5 vector, which contains SARS-CoV S nanoparticles produced in the baciculovirus insect cell expression system.	Phase-1(NCT04313127)
Moderna corona virus	National institute of health(INH),US	mRNA based vaccine, which encoded spike protein encapsulated in lipid nanoparticles.	Phase-1 (NCT04283461) and Phase-2(NCT04405076)
DPX-COVID-19	IMV(Canada)	Containg peptide epitopes from SARS-CoV-2-S Protein	Pre-clinical study
COVID-19 Vaccine	BioNTech/Pfizer(Germany)	Lipid-based nanoparticles(LNP) combined mRNA.	Phase-I/III (NCT04368728)
NVX-CoV2373	Novavax,US	Containg SARS-CoV protein combined with adjuvant matrix-M	Pre-clinical study
COVID-19 Vaccine	BIOCAD (RUSSIA)	LNPs with recombinant S protein & epitope from SARS-CoV-2	Pre-clinical study
COVID-19 Vaccine	University of Tokyo(Japan)	LPNs combined with mRNA.	Pre-clinical study

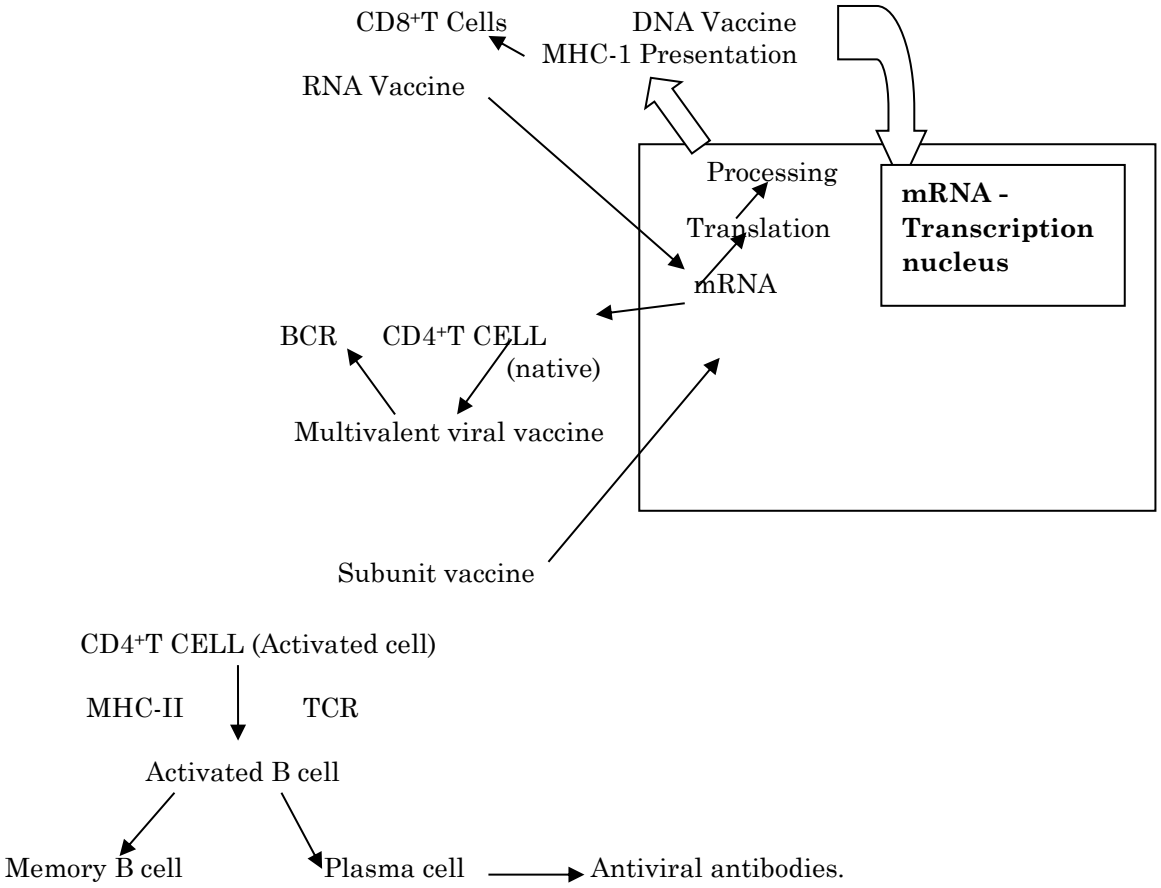

Fig-2: Vaccine processing and immune response [11]

This schematic diagram display key steps involved in nanoparticles based vaccine processing by APCs. APCs with epitope are presented by MHC-1 and MHC-2 leading to produce CD^{8+} cytoxic T cell or CD^{4+} helper cell required for antiviral antibody production.

ROLE OF NANOTCHNOLOGY IN COVID-19 OUTBREAK

Nanomedicine strategies are in use for the design of the vaccine carriers but this nanomedicine is only enough comparision to other nanotechnology approaches being explored to tackle the current outbreak.

Similarly the vaccine development holds significant commonalities with strategies explored against previously known SARS, MERS coronaviruses. Based on the antiviral and biomolecular delivery having some limitation is that poor aqueous solubility, low-bioavailability can be solved by nano carrier based antiviral drugs delivery, pharmacokinetics /pharmacodynamics properties and resulting in dose reduction, reduce toxicity and improved drug bioavailability and maintenance of the suppression of viral spread. Controlled or sustained releasing nanocarriers are the best solution to mitigate the risk effects of poor patient compliance viral rebound during the treatment of viral infections.

The role of nanocarriers technologies is decisive in the development of RNAi, nABs, protein, peptide and other biologics. Nano carriers based delivery ensure improved half-life the biologicals by preventing premature drug release and degradation along with evasion of renal and hepatic clearance.

Targeted nanoparticles provide an improved rate of endocytosis which better ensures delivery of a therapeutics nanoparticle dose to the target cell [9]. Nanotechnology an excellent tool for vaccine development.

Antigen protection from premature degradation to enhance immunity response, reduce adverse effects, deliver site-specific antigen and facilitate intracellular uptake. Organic NPs have been used in vaccine development like liposome are most popular nanoparticle clinically approved used in hepatitis A, and influenza A and B. Biopolymer based like protein based polymer used in lower toxicity and bio-degradability.

Virus-like proteins (VLPs) are formed by viral proteins display a high density of epitope. Apartment from that lack any viral DNA/RNA, which makes them non-infectious. So that non-protein antigen coupled to the surface, it induces cross-protection against different viruses [12].

Other nanotechnology-based systems have been used as carrier & adjuvants in the development vaccines. Conjugation of metallic NPs with viral antigen to produce specific antibody.

Example-Aluminium is metallic NPs used in vaccine for MERS-CoV and SARS-CoV as respiratory pathogen, inducing both humoral and cellular immune response. Cell-membrane based structures are also used antibacterial and antiviral vaccines.

Aluminium NPs were used as vaccine adjuvant delivery system for pulmonary immunisation using oval aluminium as model antigen, improving lymph nodes.

This strategies addressing nanotechnology is a promising tool for targeting vaccine against pathogen microorganisms (SARS-CoV, MERS-CoV) to the respiratory tract. All the above demonstrate potential nanotechnology to design effective immunisation strategy [13].

NANOMEDICINE APPROACH FOR VACCINE RESEARCH IN COVID-19

One of the bigger challange in the covid-19 vaccine research is to identify approaches that stimulate both T and B cell against this virus. Apart from that necessity of accelerating the development of precise next generation vaccine strategy that may also address specific population subgroups with compressed immunity.

The nano vaccine strategy also requires a strong focus on the cellular presentation of the selected antigen, along with the selection of appropriate nanomaterial to induce complimenting immunomodulatory effects.

Table 2: Rational selection of drug nano-carrier combination [14]

Combination description	Combination treatment	Study status
Non-nucleoside reverse transcriptase inhibitor + Nucleotide reverse transcriptase inhibitor	Tenofovir + Emitricitabine	Under trial of COVID-19
Nucleoside inhibitor + protease inhibitor	Ribavirin + Ritonavir	Clinical study of SARS
Protease inhibitor	Ritonavir+ Lopinavir	Under trial of COVID-19
Protease inhibitor + Protein released by host cell	Lopinavir+ Ritonavir+ IFN Beta 1b	Clinical study of MERS
Protease inhibitor + Protein released by host cell + Antiviral	Lopinavir+ Ritonavir+ IFN+ Ribavirin	Clinical study of MERS
Antiretroviral protease inhibitor	Darunavir+ cobicistat	Under trial of COVID-19

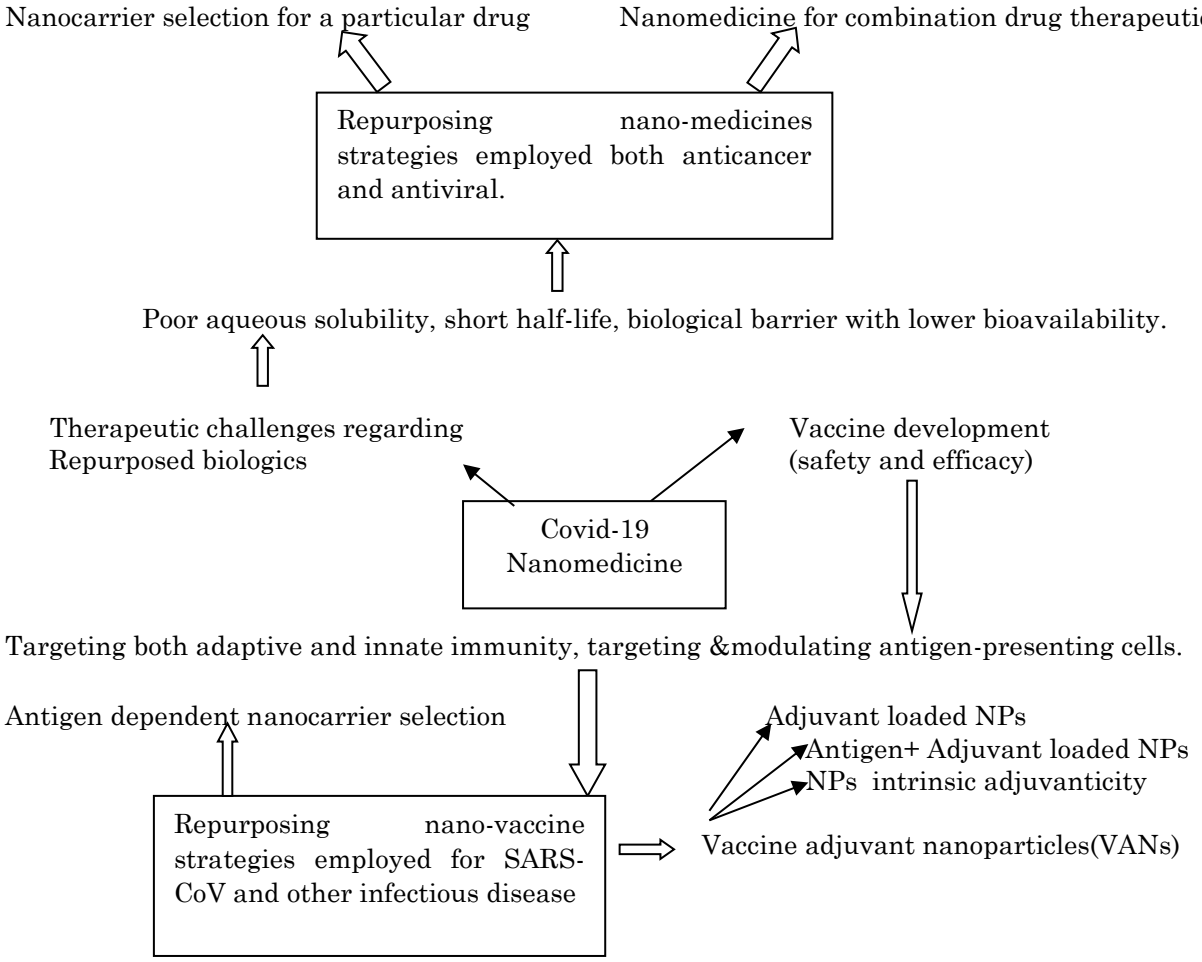

Fig. 3: Nanomedicine approach for COVID-19 vaccine development and therapeutics [15]

RATIONALE DESIGN OF NANO CARRIERS BASED VACCINE WITH TWO STRAT4EGIES

Strategy-1 Antigen-Dependent Nanocarriers Selection:

Presence of antigen inside the surface of nanocarriers is depend upon several factors like biological stability, target sites and required immunogens release rate of antigens. Adsorption of antigen in the surface of nanoparticle is based upon charge and noncovalent hydrophobic interaction.

Amphoteric nature of antigen are most suitable for adsorption or surface immobilisation on nano carriers such as chitosan and dextran sulfate based polymeric nanoparticle, inorganic nanoparticles and carbon nano tubes.. Antigen is designed based upon on the properties of the biological environment like pH, ionic strength, temperature etc.

Encapsulation and matrix entrapment of the antigen within a nanocarrier is one of the technique to prevent biological degradation.eg-poly lactide co glycolipid nanoparticle is ideal encapsulated antigen and provide extend biological release.

Naked mRNA are sensitive to degrade by extracellular RNAase so that formulating its delivery vehicle essential. So that mRNA based covid-19 vaccine is already under preclinical trial employing LNPs as a carrier.

LNPs are virus sized particle synthesized by self-assembly of an ionisable cationic lipid different nanoparticles of these cationic lipids such as dioleoyloxy-3-trimethyl ammonium propane/ diolylphosphatidyl ethanolamine are formulated with suitable modification (cationic lipid+ cholesterol+ PEG-LNP) whereas cholesterol used as increase the

stability and PEG (poly ethylene- glycol) lipids to increase half-life.

They ability to deliver mRNA efficiently to cytoplasm, presence of exogenous mRNA in cytosol trigger translation into fully functional protein. As like as cationic polymer based nanocarriers for DNA vaccine design are chitosan nanoparticles and polyethylenimine nanoparticles.

DNA also degrade by nuclease incomplete delivery to immune system, cationic based lipids, synthetic and natural polymers, inorganic particles are proposed for formulation of DNA vaccine.

Polymeric nanocarriers encapsulated DNA to prevent biological inactivation and controlled release to and targeted cell delivery. If employment of polyethylene glycol as nanoparticles prevent nonspecific protein interaction, reduce systemic toxicity and improve stability.to improve DNA/mRNA to across the cell membrane electroporation and gene gun method is applicable.

In third method induce pore in the cell membranes to insert the dsDNA to elicit b cell & t cell response. .An ongoing clinical trial is using a DNA plasmid encoding SARS-coV-2 Protein as a vaccine candidate for intradermally administered using an electroporation device [16, 17].

Strategy-2- Vaccine Adjuvant Nanoparticles (VANs)

Vaccine adjuvants are critical to reducing the required antigen dose permitting the production of more units and available to larger population, damage associated molecular pattern are recognized by specific receptor called pattern recognition receptor.

Example-Toll like receptor which regulated by immune cell to upregulated robust T and B cell priming by releasing inflammatory cytokines. Vaccine can either act as a nanocarrier for molecular adjuvant or have inherent physicochemical property to stimulate or anti-immunity pathway.

Vaccine adjuvant nanoparticles are designed to tackle the limitation related to conventional delivery such as rapid blood stream clearance systemic distribution as well as antigen-adjuvant localisation. Lymph nodes targeting of VANs may enhances its adjuvancity. *In vivo* study demonstrates against infectious challenge in PLGA and calcium phosphate nanoparticle co-encapsulating both antigen and adjuvant to improve efficacy by enhancing antigen uptake, APC activation.

Synergized activation of apc and prolonged antibody response was observed with the codelivery of TLR4 and TLR7 small molecule adjuvants using PLGA nanoparticles .VANs are also employed to co-deliver self-antigen or immunoregulatory drugs as adjuvants to induce antigen specific peripheral tolerance of auto reactivate T cell and block any serious auto-immune response.

Nanoparticles are also considered as VANs because activation complements system, inducing autophagy and activation of inflammasome.

Adjuvanticity due to surface chemistry and hydrophobicity. Increased side chain hydrophobicity of poly nanoparticles displayed augmented uptake DCs activation. Immune senescence is flagged with a significant decrease of immuno globulin M, interferon, T cell count, rate of cell division and proliferation, chemotaxis of neutrophils and phagocytosis [18].

SCOPE OF MISCELLANEOUS NANOTECHNOLOGY APPROACHES

The scope of nanotechnology not limited to vaccine research other approaches like covid-19 therapeutics. Targeted surface liposomes with antiviral antibodies constituent an effective strategy to

provide protection against the infection of coxsackie A-21 virus. A virus spike protein mimicking a multi valent binder that can bind to the virus in a distinct multivalent mode and inhibit its infection like that mosquito host cell membrane wrapped nanodecoys are employed to trap the ZIKA virus and effectively prevent host cell infection [12]. Carbon nanotubes and graphene nanoparticles may be interesting treatment against COVID-19, improve effectiveness of therapeutic agents [16].

Antioxidant polymeric nanoparticle mostly used in pulmonary drug delivery system. This system having excellent bio-compatibility and degradation rate. Here polyoxalate is nanoparticle and hydroxy benzyl alcohol is biodegradable agent. Polyoxalate ester linkage capable reacts with hydrogen peroxide, reducing the generation intracellular oxidative stress, expression of pro-inflammatory mediators like nitric oxide synthase, cyclooxygenase-2 and interleukins in stimulated macrophases [19].

NANOTECHNOLOGY IN THE TREATMENT OF CORONAVIRUS INFECTION

Numerous nanoscale antiviral materials have been designed to inter fere with the virus and cell receptor interaction. As mentioned above current covid-19 therapies are deduced from MERS-COV, SARS-COV and H1N1 influenza which are a combination of different antiviral agents including protease inhibitor, nucleoside analogue and corticosteroids. Nanodecoys nanotechnology is used for

- Targeted delivery of pharmacological agents to the sites of infections
- Prolong drug release for efficient treatment
- Decreasing the drug toxicity and associated side effects
- Improvng the drug efficacy and potency
- Delivery gene immune based therapies
- Targetingthe virus entrance mechanism

Recently led compound is boronic acid, the ability of carbon quantum dots to interfere with HIV-1 and herpes simplex virus type-1 cell entrance has led to the use of boronic acid functionalised CQDs for the treatment of HCoV infection. Consequently boronic acid functionalised CQD might be regarded as therapeutic agents for covid-19.

Most of the reported antiviral nanomaterials are spherical, non-spherical nanomaterials may display higher antiviral effects compared to the spherical peers. Apart from interfering with protein s-receptor interaction, NPs have been applied to target vacuolar ATPase activity, which pumps proton into endosomal compartments [20].

NANOTECHNOLOGY IN ELECTROCHEMICAL SENCING OF CORONAVIRUS INFECTION

One of the conventional method is electrochemical sensing include transduction element, electrolyte, diffusion barrier and counter reference electrode resulting electric signal from the interaction of target analyte and recognition layer is sensing electrode. The electrochemical sensing immunosensor are comprised of an electrode surface immobilisation with recognition component, efficient platform for detection of viral infection.

The addition of constant concentration antibody to the sample containing free virus immobilised MERS-CoV protein changed into the voltametric response which can be, ensured by square wave voltammetry [21].

Fascinating properties of NPs like both metallic and semiconductor including catalytic properties to use in enrichment of electron transfer, effective catalyst, surface immobilisation of biomolecules. In addition to quantum dots and gold nanoparticles employed for the

development of biosensors, Roh developed a biochip through modification by SARS-

CoV N protein and quantum dots conjugated RNA oligonucleotide and inhibitor screening of SARS-CoV N protein ability tp fabricated biochip using polyphenolic compounds.NP-based biosensors (NBS) with reverse transcription loop mediated isothermal amplification(rt-lamp) for detection of COVID-19 and sensitive detection of SARS-CoV-2 [22].

NANOTECHNOLOGY IN CALORIMETRIC DETECTION OF CORONA VIRUS INFECTION

Calorimetric biosensor are sensitive, selective and low cost detection tools capable of detecting analytes based on colour changes that can be easily recognised by naked eyes or simple portable optical detectors. Surface Plasmon Resonance (SPR) is generated by the incident light on a metal surface, causing collective coherent oscillation of conductance electrons. The SPR can be affected by shape, size and the dielectric constant of metal and the distance among the NPs.

A combination of thiol-modified probe and AuNPs at the presence of $MgCl_2$ led to the aggregation of AuNPs with a reduction in intensity and increase in bandwidth of LSPR band as well as the emergence of new bands at a longer wavelength.

The presence of target DNA led to the formation of long assembles of dsDNA on the surface of AuNPs and shielded disulfide bands leading to inhibition of the AuNPs aggregation by $MgCl_2$ which limited the color change for diagnosis of MERS-CoV. Other System such as fibre optic biosensor to achieve sensitive virus detection.

In comparison to localised surface plasmon-coupled fluorescence (LSPCF) fibre optic biosensor utilising AuNPs for detection of SARS-CoV N protein to ELISA towards the same monoclonal antibodies [23, 24].

NANOTECHNOLOGY IN RT-PCR BASED DETECTION OF CORONA VIRUS

RT-PCR is the main conventional diagnostic method for CoV infection. This method requires the extraction of high-purity nucleic acids to produce strong signal and low false negative results. This method useful for the extraction of nucleic acid using filtration or centrifugation are very time consuming, labor intensive.

This method is superior over conventional procedures due to shorter processing times, decreased chemical consumption and sampler procedure via automation. Poly amino ester with carboxyl group coated magnetic NPs for the extraction of SARS-CoV-2 RNA, resulting in the sensitive detection of COVID-19 via RT-PCR. Comparison between column based nucleic acid extraction method showed rapid simple extraction with high purity and productivity with assistance of an external magnet, resulting in time consuming RNA extraction for the diagnosis of covid -19 [25].

Gold Nanoparticles: Recent study about both in vivo and invitro method AuNPs link with sulfonate mercapto ethane sulfonate (MES) and undecanesulfonic acid(MUS) caused irreversible deformation in several multivalent binding to the virus collapses the capsid structure.. One of the important strategy for therapy in COVUD-19.

Gold nanostructures are versatile platform for biomedical application. Novel surface engineered gold Nano rods used as DNA vaccine adjuvant for HIV treatment. Surface chemistry on the adjuvant activity of the gold nanorods by placing three types molecule such as (CTAB) cetyl trimethyl ammonium

bromide,(PDDAC) poly diallyl dimethyl ammonium chloride and (PEI) polyethyleneimine on the surface of nanorod [26].These molecules modified Au NRs can significantly promote cellular & humoral immunity as well as T cell proliferation by activating Antigen Presenting Cells. Comparison between Surface-Engineered Gold Nanorods to DNAvaxcine adjuvant for HIV-1 in vivo study. Result is that rational design of low toxic- nanomaterials as a versatile platform for vaccine nano adjuvants system [27].

Silver Nanoparticles- The prime advantages are of AgNPs is used as antiviral agents without surface modification. AgNPs has focused on optical, electrical, thermal properties and as antimicrobial activities. Main limitation is that silver nanoparticle might bind with glycoproteins on the virus surface, preventing genome replication & preventing virus ion fusion. To overcome this situation poly vinyl alcohol (PVA), Poly vinyl pyrrolidine (PVP) can be used as coating materials show antiviral activity on HIV-1 strains [28].

Mesoporus Nanoparticles: (MSNPs) this NPs having dual characteristic means it allow accommodating molecule inside and outside for co-delivery could provide an excellent platform to treat COVID-19 that means several ligands to inactivate the entry of the virus in the host cell and to the site specific release of these ligands, preventing viral replication. Simultaneously ion the early stages of viral internalisation and DNA replication occurs [29].

Iron oxide Nanoparticles: it is widely used in biomedical approach mainly applicable magnetic resonance imaging. Mannose loaded iron oxide NPs were delivery in dendritic cell (DC) LIKE AS il-6, tnf-alpha and IFN-gamma was observed in DC in comparison to the IONPs without mannose in vitro studies. In vivo studies also showed higher levels of TNF-Alpha, IL-2, IL-4, IL-12 and INF-gamma using mannose loaded IONPs. Organic Nanoparticles-carbon nanotube and graphene nanoparticles (CNTs). CNTs with hyaluronic acid increases interaction of nano-system with bronchial cells & prevents the inflammatory process in the pulmonary tissues resulting CNTs modification with cellular ligands increases NPs uptake and drug release at targeted tissues by endocytic absorption without plasmid membrane damage [30].

Dendrimer Nanoparticles: It is one type of revolution in nanotechnology as novel carrier to improve efficiency of drugs and bioactive compounds. Structurally looks like as three dimensional structure ability strong interaction between virus so increase antiviral activity in vitro study the first polycationic dendrimer based on primary amine to asses antiviral activity against MERS-CoV, that is only possible effect of dendrimer size and terminal charge on the ability of MERS-CoV.

Develop synthetic, single dose, adjuvant free dendrimer nanoparticle platform where in antigens are encoded by encapsulated mRNA replicons. This NPs generating protective immunity against lethal pathogen including H1N1 influenza, Ebola virus, capable eliciting both CD8+ and T cell and antibody response [31].

Lipid-based Nanoparticles: This NPs already explored in the treatment of HIV, HCV, HBV, herpes viruses because they encapsulate different classes of antiviral drugs, modulating biological response and mediating the delivery from the administration site to target site. Different types of lipid raw material can be employed in the development of nanocarriers such as phospholipid, fatty acid, mono-, di-, tri glycerides which assemble in water to produce different structured systems to show both hydrophobic and amphiphilic nature [32].

Ferritin: Ferritin is composed of 3-fold axis symmetry, 24 alpha helix subunit with improved thermal and chemical stability. Conformation of ferritin nanoparticles show of trimeric antigens providing cross-protection against different subtype of influenza virus. Ferritin nanoparticle display viral glycoprotein by genetically fused in hemagglutinin at the interface of ferritin NPs without compromising native trimeric conformation.

In comparison to current commercial vaccine these nanoparticles to enhance the potency of neutralising antibody response, provide protection against H1N1 viruses in ferrets. Structure based development of ferritin nanoparticle consisting of only H5N1 viruses in ferrets, H5N1 neutralising activity detected in vitro but in Hemagglutinin stem based vaccine provide protection without need of using the same neutralising epitope [33].

CONCLUSION

Recent research into the use of metal nanoparticles as antimicrobial agents can improve new solution for surface recognition &enhances efficacy of PPE product. Nanoparticles play a pivot role in COVID-19vaccine development & involvement of high-tech platforms such as viral vector, antigen carriers & delivery technology.

A mRNA-based vaccine employing LNPs delivery where as another is electroporation technology for the intradermal administration of DNA plasmid. Rational designing of nanocarrier-based vaccine is equally importance to the selection for antigen loading & effectively delivery. Miscellaneous technologies based on functionalised CQDs biomimicking scaffolds are present the scope of unconventional therapeutics.

Nano-based formulation also designed to target a specific tissue with c0ntrolled release properties which increase efficiency of treatment. One of the major challenge is to ensure the safe use of nano material, evaluate the biocompatibility using in vitro approach. In vivo models need to better understand toxicokinetic behaviour of the nanoparticles in the body especially long term exposure. Both protein-nanoparticle and protein-protein interaction regulate the adsorption of protein on the surface of nanoparticles.

The formation protein corona modifies the physicochemical properties of nanoparticles, gives to new biological identity which is more significant than the properties of the original properties of nanoparticles.covid-19 specific feature and physiological properties of the nano-system, seeking to neutralize the current threat to global public health and create more sustainable approach based on nanotechnology.

In the last several years significant progress in the use of nanoparticles as vaccine delivery platforms. Both organic and inorganic nanomaterials having unique advantageous properties as vaccine carrier.

FUTURE PERSPECTIVE

Nanotechnology is combination therapy aim for repurposing and designing of particles. Nanotechnology has established a new and mighty era in the diagnosis & treatment of viruses, including COVID-19.Clinical application may focus on safety, dose-response and size-efficiency of nanoparticles.

Designing nanoparticle platform to diagnose and limit triggering of tissue damage cascade in human cell is necessary because strategies to manipulate virus structures and their enzymes by NPs is crucial .Modification of nanoparticle enhances circulation time, drug entrapment efficacy, bio distribution and drug metabolism. Advanced methos such as molecular dynamics, docking and micro-fluidic predicting virus-NPs interaction will be valuable study.

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