SCOPE OF NANOMEDICINE AND NANOTECHNOLOGY IN THE NOVEL PADNEMIC DISEASE- COVID 19

ABSTRACT

The pandemic of coronavirus disease 2019 (COVID-19), triggered by the extreme acute respiratory syndrome coronavirus 2 (SARS-CoV-2), started in Wuhan , China in December 2019. To date, the number of people has been infected by the virus, causing approximately number of people deaths worldwide. Person-to - person transmission of COVID-19 infectionresulted in the isolation of a variety of therapies from patients who were subsequently given. The current emerging COVID-19 pandemic has caused a global impact on every major aspect of our societies. Perspectives on how biosensors, vaccines, and antiviral nano systems can beapplied to combat COVID-19 are envisaged; defining short-term methods that can be applied and those that require long-term study to deal with potential pandemics related to respiratory viruses . We review current approaches to the creation of COVID-19 vaccines here and highlight the role of nanotechnology, nanomaterials, diagnosis of COVID-19 and treatment will used for the future prospective.

Key words: Coronavirus, Mechanism, Global Scenario, nanoparticles, antiviral agent, diagnosis, Treatment.

INTRODUCTION

OVERVIEW ON CORONAVRUS

Coronaviruses are single-stranded RNA viruses that are spherical, enclosed, and belong to the subfamily Coronavirinae of the family Coronaviridae (order Nidovirales).[1]

The first epidemics of the novel coronavirus infections (COVID-19) were discovered in the seafood sector. In mid-December 2019, it had spread to 214 nations, territories, and places globally from Wuhan City in China's Hubei Province..[1,2]

One of the main infections that primarily affects the human respiratory system is the coronavirus. Coronaviruses are vast group of viruses that cause sickness in humans and animals. Rarely, animal coronaviruses can develop, infect humans, and then spread to other humans as was the case with the spherical, enveloped, and single-stranded RNA-based Middle East respiratory sickness (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV) viruses.[3,4]

It resulted in almost 10,000 cases overall over the previous 20 years, with fatality rates of 10% for SARS-CoV and 37% for MERS-CoV. Soft tissues like the lips, eyes, and nose are where the infection can spread. SARS-CoV-2, a single-stranded RNA virus with a short genome of 26–32 kb and a diameter range of 65–140 nm, is the pathogen. The virus was initially identified as the 2019 new coronavirus by Chinese researchers (2019-nCoV).

The WHO named the 2019 new coronavirus (COVID-19) on February 11, 2020, causing a coronavirus outbreak. The estimated reproduction number was slightly higher than 1. (range from 2.24 to 3.58).

HOW CORONAVIRUS INFECTED AND DAMGE THE HUMAN BODY

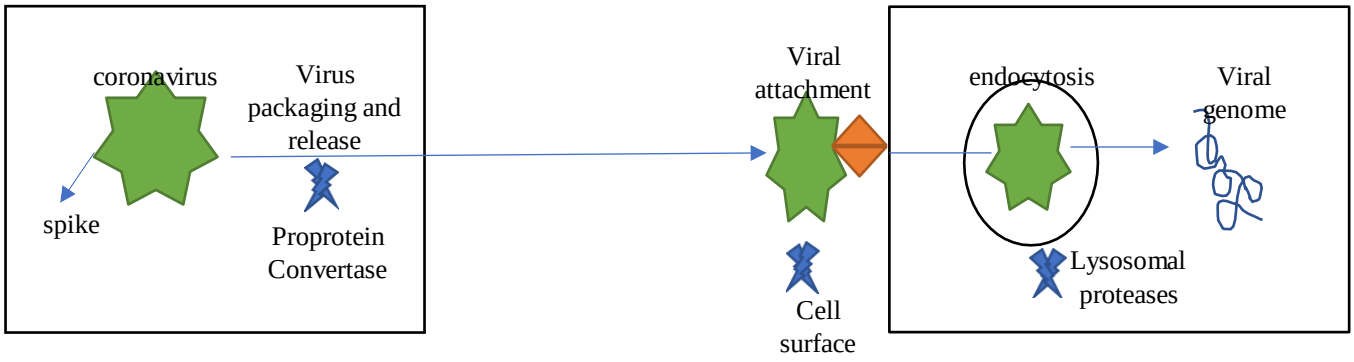
Some scientists have identified two unique types of cells in a human nose that are the initial infection points in a human body after continuous study to understand how the novel Coronavirus affects humans.[5]

Mainly the two cells-goblet cells and ciliated cells are two kinds of cells where the SARS- CoV2 entry process takes place and the virus starts to attack, according to a study by The IndianExpress. [6]

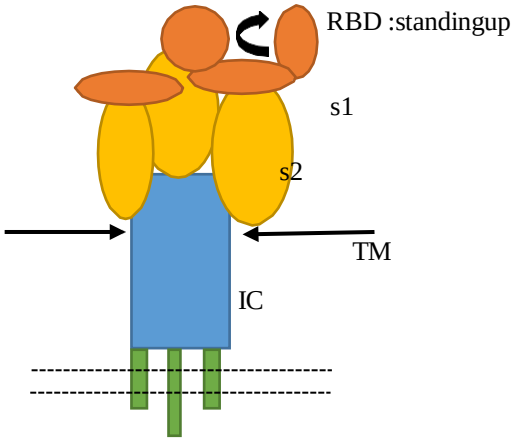
This study, the report said, has been identified by researchers in University Medical Centre Groningen, Welcome Sanger Institute (UK), University Côte d'Azur and CNRS, Nice. To be sure, Goblet cells are those that produce mucus within the nose and are found alongside the respiratory tract. Ciliated cells, on the other hand, are hair like cells that help sweep mucus or dust to the throat.

Now what actually happens is that the report said, the virus has a lock and key effect. This unique virus has a fatty envelope on the surface containing a spike of protein. This protein unlocks another protein (ACE2) that is present on the human cell.

After this is unlocked, the virus enters the human cell. There it uses a second protein called TMPRSS2 which allows the virus to reproduce and eventually leads it to the transmission within the cell.


coronavirus
spike
Virus packaging and release
Proprotein Convertase
Viral attachment
Cell surface proteases
endocytosis
Viral genome
Lysosomal proteases
Virus-producing human cell
Virus- targeted human cell

(A)


RBD :standingup
s1
s2
TM
IC

(B)

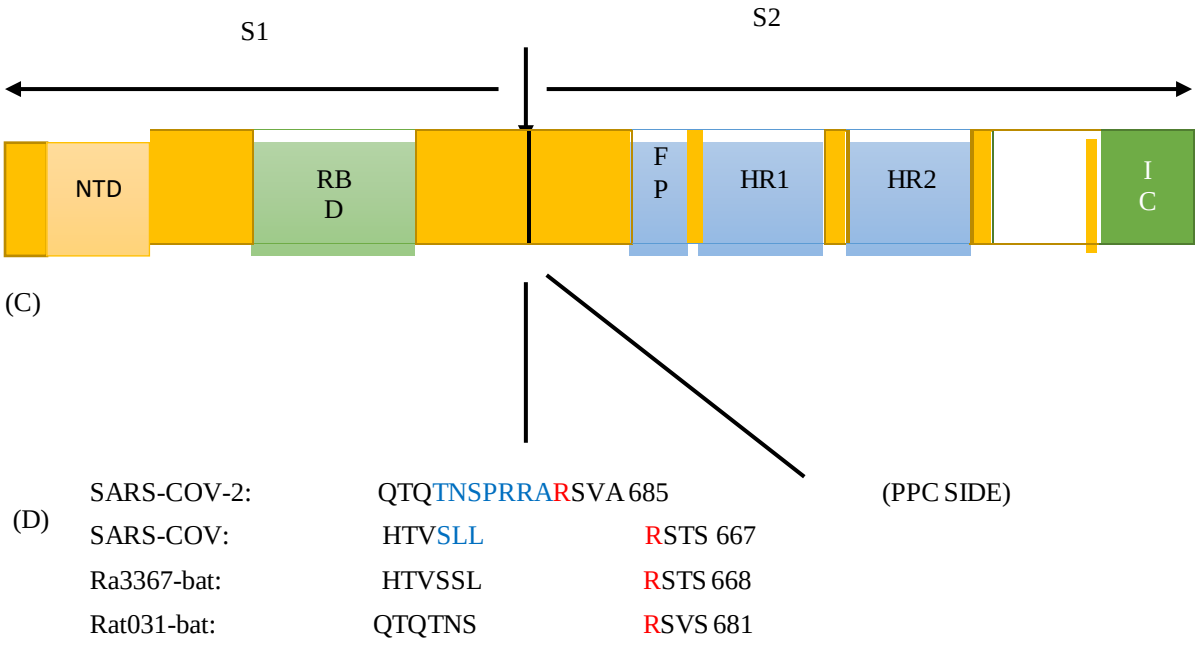


Fig.1 shows the how corona viruses targeted the human cell

A. Different stages of coronavirus entry where host cellular proteases may activatecoronavirus spikes.

B. Schematic drawing of the three-dimensional (3D) structure of coronavirus spike. S1, receptor-binding subunit; S2, membrane fusion subunit; TM, transmembrane anchor; IC, intracellular tail.

C. Schematic drawing of the 1D structure of coronavirus spike. NTD, N-terminal domain. FP (fusion peptide), HR1 (heptad repeat 1), and HR2 (heptad repeat 2) are structural units in coronavirus S2 that function in membrane fusion.

D. Sequence comparison of the spike proteins from SARS-CoV-2, SARS-CoV, and two bat SARS-like coronaviruses in a region at the S1/S2 boundary. Only SARS-CoV-2

E. spike contains a putative PPC motif—RRAR (residues in the box).

SYMPTOMS:

The most common symptoms at onset of COVID-19 illness are fever, cough, and fatigue,while other symptoms include sputum production, headache, haemoptysis, diarrhoea ,dyspnoea, and lymphopenia, conjunctivitis, aches or pain, and serious symptoms are difficulty beathing or shortness of breath, chest pain or pressure, loss of speech ormovement.[7–9]

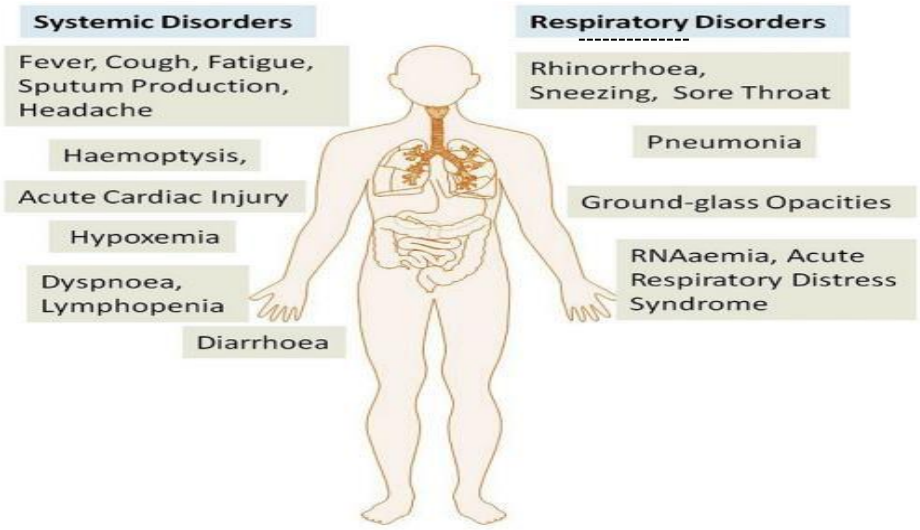


Fig 2 show the systemic and respiratory disorders of the COVID-19

GLOBAL SCENARIO

Covid-19, just few months back, corona virus was start in December 2019, Wuhan city whichis located in china. Now a days its spread all over in world, its Starting with one case and nowwith millions of cases.[10,11]

The most ten country which highly affected with COVID-19 is the first highest country is **United States** which having 7.11 million novel coronavirus cases, the second worst affected country is **India** which having the 6 million novel corona cases, Third, in the list of the worst affected country is **Brazil** with more than 4 million corona cases, **Russia** reported more than

1 million cases of coronavirus infection**. Colombia** with more than 8 lakh coronavirus cases, **Peru** reported 8 lakh coronavirus cases, **Mexico** now has 730,317 confirmed cases of coronavirus**, Spain has** 716,481 coronavirus cases, **Argentina** COVID-19 death toll rises to 15,749**, South Africa** reported 670,766 coronavirus cases, all updates provide until October 2020.[12]

The ten Countries with **no recorded Covid-19** cases which are **Palau, Micronesia, MarshallIslands, Nauru, Kiribati, Solomon Islands, Tuvalu, Samoa, Vanuatu, Tong.**

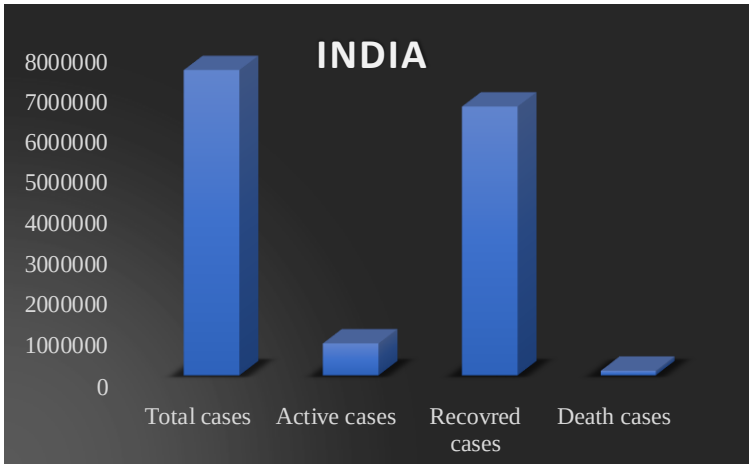


Fig.3 show the graphically represented the update of COVID-19 in india till october 2020

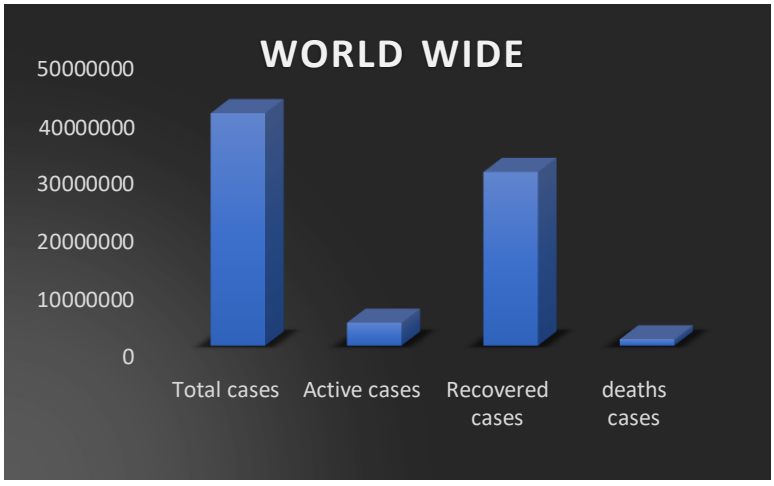


Fig.4 show the graphically reperesented the update of COVID-19 in world wide till october2020.

Above both graph show the latest upadte on corona virus diesease who are infected and recoverwith these diesease.

In India most five state which is highly affected with COVID-19 is **Maharashtra**, **tamilnadu,Andhra Pradesh**, **Karnataka**, **Uttar Pradesh.**

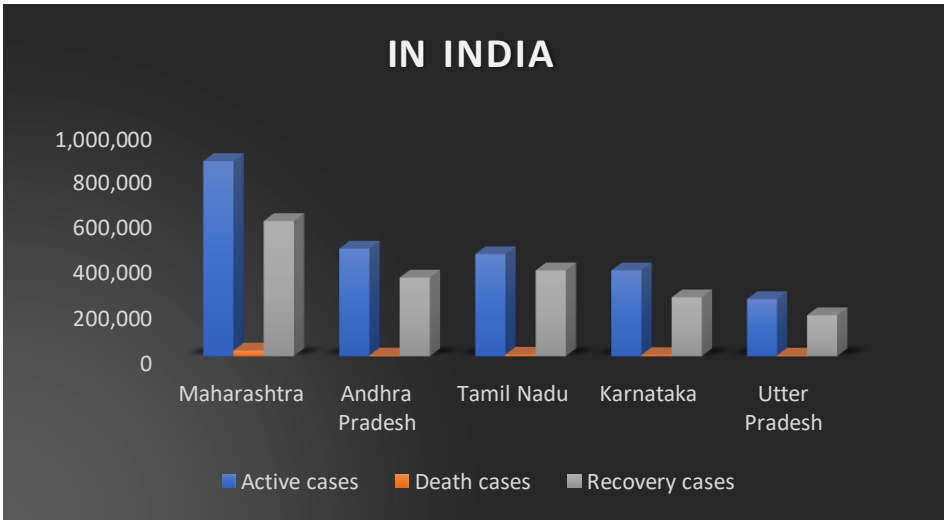


Fig.5 show the graphically represented the update of COVID-19 in India with highly affectedstate with till October 2020

OVERVIEW ON NANOPARTICLES

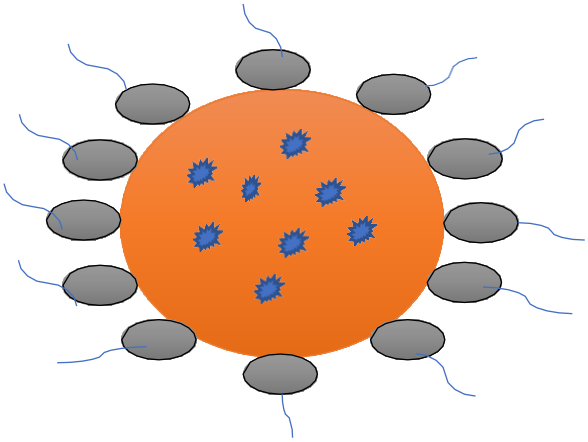
A nanoparticle is a small particle that ranges between 1 to 100 nanometres in size. Undetectableby the human eye, nanoparticles can exhibit significantly different physical and chemical properties to their larger material counterparts.[13]

Nanoparticles are small but have a large ratio of surface to volume which gives themphenomenal, distinctive characteristics. Because of these characteristics, nanoparticles have been used and are treated as a bridge between bulk material in the field of biotechnology, medicine, drug delivery, sensor, and DNA labelling and are treated as a bridge between bulk materials.[14]

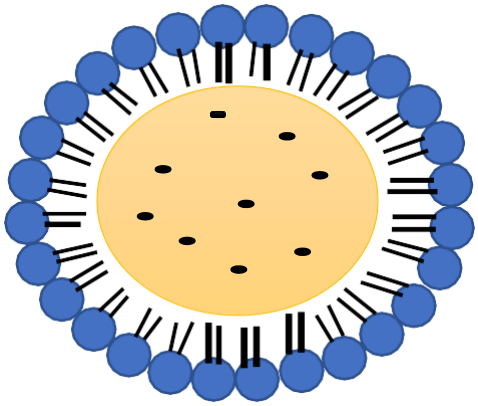
Nano approaches have been used widely used to improve the distribution and efficacy of antiviral drug, particularly with nucleoside analogues in conjunction with delivery system thathave potential application against drug resistant human immune deficiency virus infection. (8)

The many available nano delivery systems can be used with newly developed drug formulations to efficiently deliver the drugs with faster therapeutic indices for COVID-19. (8)

Types of nanoparticles (10)



(A)



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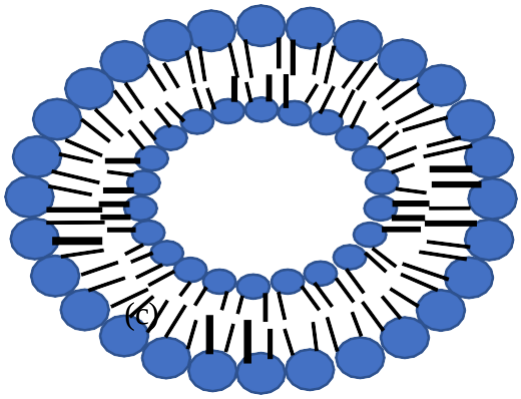

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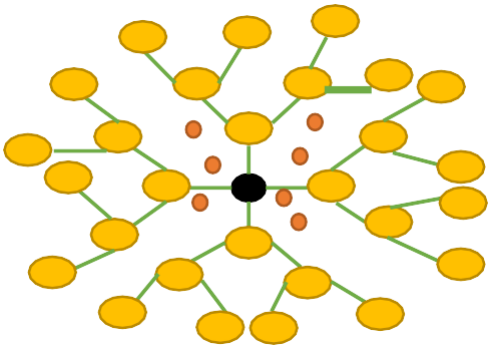

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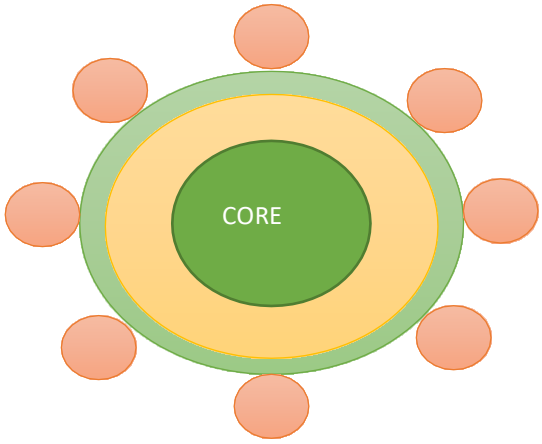

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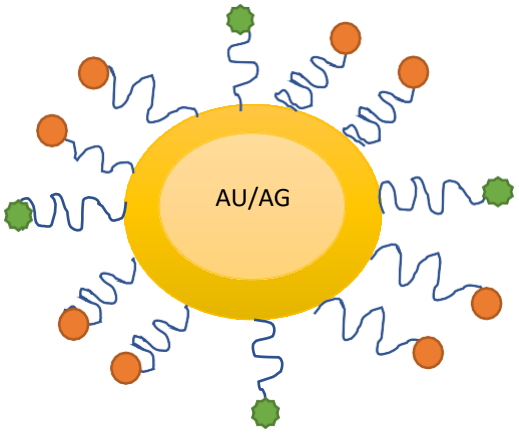

(F)

Fig 6 show the types of nanoparticles

(A) Polymeric nanoparticles

(B) Solid lipid nanoparticles

(C) Liposomes

(D) Dendrimers

(E) Quantum dot

(F) Metallic nanoparticles

NANOPARTICLES REPORTED AS AANTIVIRAL DRUG

In recent years, nanoparticles have become increasingly popular as drug delivery system for their many benefits including managed drug release, defence against degradation of active molecules and cell targeting.

They have been proposed as carriers of antiviral drugs for increasing their therapeutic index. Nanoparticulate-based systems may change the release kinetics of antivirals, increase their bioavailability, improve their efficacy, reduced adverse drug side effects, and reduce treatmentcosts.

In addition, they could allow antiviral drugs to be delivered to specific target site and viral reservoirs in the body. these characteristics are especially important in viral diseases, where high doses of medicinal product are required and where many active molecules are low in bioavailability. [15–18]

Currently, nanoparticles are known to exert their antiviral activities by various mechanisms.
First, the unique properties of nanoparticles such as, [19,20]

(1) small particle size (which can facilitate drug delivery into anatomically privileged sites),

(2) Large ratio of surface area to volume (which ensures that large drug payloads can beaccommodated), and

(3) tunable surface charge (to allow cellular entry across the cell membrane that is negativelycharged) make nanoparticles attractive tools for viral treatment.

Second, it has been shown that biomimetic properties can be present in nanoparticles can be present in nanoparticles, resulting in intrinsic antiviral properties. silver nanoparticles and dendrimers are popular examples of these.

Third, optimized drug dosing and enhanced distribution by increasing stability and retention times may all contribute to the possibility of drug encapsulation functionalization by creating stable structure or modification with polymers such as polyethylene glycol.

Finally, is assumed that by designing nanoparticles with targeting moieties to increase specificity to desired cell type, target tissues or subcellular compartment, drug delivery can begreatly improved.[19]

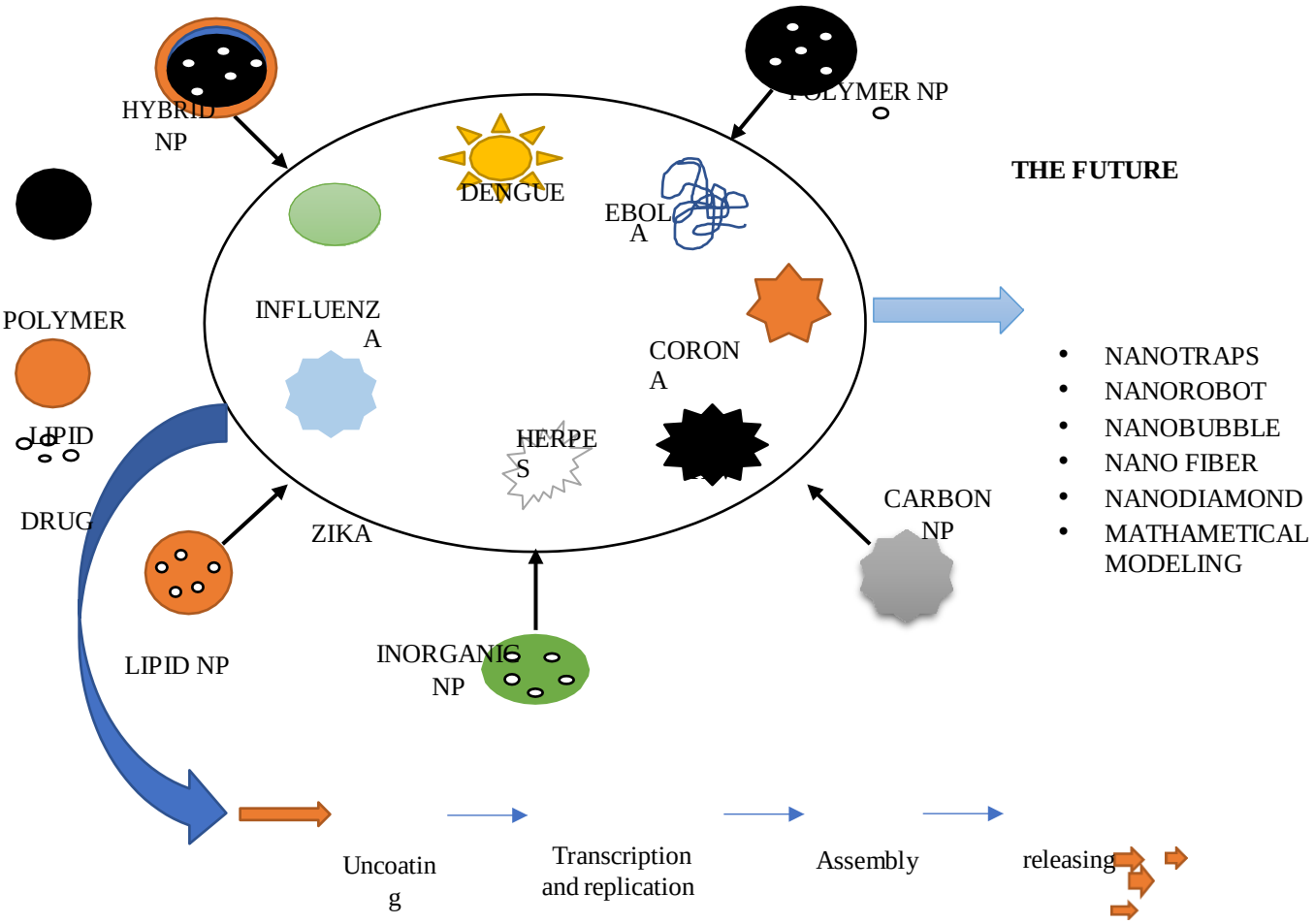

Fig.7 shows the role of nanoparticles in the viral diseases

In the future nanotraps, nanorobot, nanobubble, nanofiber, nano Dimond, mathematicalmodelling is used in the treatments of viral infection like influenza, dengue, Ebola, corona, HIV, herpes, zika viruses.

1. ROLE OF NANOTECHNOLOGY USED IN DIAGNOSIS OF COVID-19

In the containment of COVID-19, diagnostics may play an important role in facilitating the rapid implementation of control measures that limit the spread by identifying and isolating cases and by tracing contact (i.e. identifying people who may have come into contact with an infected patient). [21–23]

Nanotechnology offers new possibilities for the development of affordable and versatile methods of detection, safe personal safety devices and new successful drugs.

Nano sensors are now a reality and can detect extremely low bacterial and viral concentrationsin patients with extremely low viral loads and thus alert clinicians even before symptoms havebeen seen. From the end of December 2019 to mid-February 2020, 104 SARS-CoV-2 viral strains were isolated and sequenced with Illumina and Oxford nanopore sequencing, accordingto the joint WHO taskforce and China. [24]

To diagnose COVID-19, various nano-based strategies have been developed, which have advantages over molecular methods. The methods currently being developed are discussed below. [3]

- Point-of-care testing
- Optical biosensor nanotechnology
- Nanopore target sequencing (NTS)
- Reverse transcription loop-mediated isothermal amplifies cation (RT-LAMP) coupledwith a nanoparticles-based biosensor (NBS) assay

POINT OF CARE TESTING

Fig 8 Instrument of piont of care testing

To treat patients without sending samples to centralized labs, point-of - care tests are used, yielding results without needing a testing network to classify infected patients. The identification of lateral flow antigen for SARS-CoV-2 is a point of care considered for the diagnosis of COVID-19.

A paper-like membrane strip coated with two lines contains commercial lateral flow assays: one contains gold nanoparticle antibody conjugates; the other captures the antibodies. Samplesfrom patients (e.g., blood and urine) are collected on the membrane and the protein is drawn across the line by capillary action. The antigens bind to the gold conjugate of the nanoparticle-antibody as the first line passes, and the complex flows across the membrane.

When they join the second side, where the red or blue side is visible, the captured antibodies immobilise the complex. Individual gold nanoparticles are red, and the plasmon bands coupledcause the solution to turn blue containing the clustered gold nanoparticles produced.

Many platforms are being developed in academic laboratories, such as electrochemicalsensors, paper-based systems, and surface-enhanced Raman scattering systems. .[3,25–27]

OPTICAL BIOSENSOR NANOTECHNLOGY

A new system based on optical biosensor nanotechnology will allow the coronavirus to be detected directly from patient samples in approximately 30 minutes without the need for centralised laboratory testing.

If an individual is infected with the coronavirus or the influenza virus may easily be determinedby this new technology.

This initiative will eventually be used to treat humans and for more than the current pandemic.The new biosensor method can also be used to examine different types of coronavirus presentin animal reservoirs, such as bats, to identify and track the possible evolution of these viruses and to avoid future human outbreaks. [3,28,29]

NANOPORE TARGET SEQUENCING (NTS)

In just 6-10 hours, the NTS system simultaneously detects SARS-CoV-2 along with ten other respiratory viruses. It is sufficient for the current diagnosis of COVID-19; however, the structure for the diagnosis of other viruses and pathogens can be extended. NTS is based on amplifications of 11 SARS-CoV-2 virulence-related and unique gene fragments (e.g., orf1ab)using an internal primary panel followed by sequencing of the amplified fragment on a nanopore platform.

This project uses a nanopore platform for sequencing, which can sequence long nucleic acid fragments and simultaneously analysed the data output in real time. This allows confirming SARS-CoV-2 infections within minutes of sequencing by mapping the sequence reads to the SARSCoV-2 genome and analysing the identity, validity and read number of the output sequence. Based on the virulence region (genome 21,563–29,674 bp; NC 045512.2) encodingS (1273 amino acids; AA), ORF3a (275 AA), E (75 AA), M (222 AA), ORF6 (66 AA), ORF7a (121 AA)

For all test samples, the NTS is performed on one Minion sequencer chip and the sequence data is analysed at regular intervals using an in-house bioinformatics pipeline. Both high identity reads were calculated by mapping output reads on the SARS-CoV-2 genome to improve plasmid concentrations. As a standard for qPCR, by evaluating only one or two sites,NTS cannot decide if a sample is positive for infection results from all target regions should beconsidered. [3,30,31]

REVERSE TRANSCRIPTION LOOP-MEDIATED ISOTHERMAL AMPLIFIES CATION (RT-LAMP) COUPLED WITH A NANOPARTICLES BASED BIOSENSOR (NBS) ASSAY

COVID-19 is a highly lethal respiratory disease that has caused international anxiety and is rapidly spreading. It is currently diagnosed via real-time RT-PCR (reverse transcriptionpolymerase chain reaction) by detecting the SARS-CoV-2 nucleic acid.

The LAMP approach is very accurate since the target sequence is identified by six or eight different regions, directly using the RNA as a reference. The results of the detection can be seen macroscopically by the change in colour.

Those techniques include amplification of recombinase polymerase, helicase-based amplification, and loop-controlled isothermal amplification. Several academic laboratories have developed and clinically validated the RT-LAMP tests for SARS-CoV-2. A one-step, one-tube RT-LAMP-NBS assay has been developed to diagnose COVID-19.

This technique is beneficial because it is easy to operate and requires only simple , inexpensiveequipment (e.g. a water bath or heating block) for 30-40 minutes to maintain a steady temperature (63 ° C). Studies have shown that NBS, a simple and easy-to-use tool, can visuallyand objectively demonstrate the effects of RT-LAMP compared to previously developed COVID-19 RT-LAMP assays, removing the need for complex processes (e.g. electrophoresis),special reagents (e.g., pH indicators) and costly instruments (e.g., real-time PCR).

In an isothermal reaction , two target sequences are amplified simultaneously and detected in the test stage.

Future studies can establish the basic theory of COVID-19 RT-LAMP, optimise the parametersof the reaction (e.g. amplification temperature) and prove its feasibility. The specificity of theCOVID-19 RTLAMP-NBS test was investigated by detecting patterns derived from different pathogens, including viruses, fungi , and bacteria.[3,32,33]

ROLE OF NANO MEDICINE USED IN COVID-19

In current situation or in a future nanoparticle are a wide range group used in the various treatment of infective disease. The goal of nanoparticles development will be giving the rapidaction to treat the diseases.[34,35]

Now a days, the metallic nanoparticles and dendrimers are used for the treat the various viral infection diseases.

Nanomedicine has an effect on all medicine fields and has been considered a significant tool or new diagnostic, medicine imaging, nanotherapeutics, vaccines and the development of biomaterials for regenerative medicine.[36]

The primary method for soft nanoparticles is to develop the biopharmaceutical, pharmacokinetic and pharmacodynamic aspects of drug loading. Specific drug targeting(passive or active targeting) and managed drug release rates may also be promoted bynanoparticles, there by influencing the effectiveness and safety of the treatment. In addition tosoft and metal nanoparticles, nanomedicines have been used mostly because of their various antimicrobial (antibacterial, antifungal, antiparasitic, and antiviral) activities. [37]

Nontechnology opens a new path for antiviral therapy in this way, considering specific targeting. Mechanisms that influence the entry of virus into the host cell before it is inactivatedmay be involved in the technique of using nanoparticles to battle SARAS-COV-2.viral surfaceprotein blockage can lead to virus inactivation, so targeted nanoparticles specific to protein expressed by viruses may decrease viral internalisation. Metal nanoparticles have shown the ability to block viral attachment to the cell surface, leading to the inhibition of viral internalization and thereby impairing the viral replication during viral entry. Nanoparticles composed of titanium (Ti), silver (Ag), gold (Au) and zinc (Zn) have already shown results against the HIV, influenza virus, herpes simplex virus, respiratory syncytial virus, transmissible gastroenteritis virus, monkey pox virus and zika virus.

The mechanism of action based on the attachment of nanoparticles to the viral envelope or itsprotein, which impairs the host cell's interaction. The effectiveness of the treatment is related to the size, shape, and surface load of the nanoparticles. but protection precautions must be taken to prevent host cell cytotoxicity in terms of concentration.

Organic nanoparticles have been used for delivering antivirals such as zidovudine, acyclovir,dipivefrine and efavirenz, remdesivir and with the aim to improve drug bioavailability and promote efficient drug delivery and targeted antiviral activity.

The versatility of nanoparticles makes them tunable vectors for virus targeting and specific drug delivery. Antimicrobial drugs have been tested in clinical trials for COVID-19, such as chloroquine, lopinavir, ritonavir, ribavirim and remdesivir, and have demonstrated promising results against SARS-CoV-2. Nanoencapsulation of antimicrobial drugs may contribute to the development of safer treatments for COVID-19 and other viral diseases.[3,34]

FUTURE PROSPECTIVE

A global health epidemic is currently threatening the world. The COVID-19 infection-to- mortality ratio has crossed boundaries, making it isolated from other viral infection. In order to resolve the danger of SARS-COV-2, physicians and scientise must work together to providesolid foundation for blocking possible pandemics. research and technology production and implementation are our best arms in the fight against COVID-19. To handle, track and preventthe spread of COVID-19, nanotechnology tools can be updated. Nanotechnology provides a specific range of resources which can contributed greatly to our knowledge of viral diseases and the to the crucial creation of diagnostic and therapeutic platforms. Together we can overcome this current pandemic to prevent and mitigate future viral outbreaks.

In the future, an ideal antiviral agent will need to exert a broad-spectrum action against virusesof different families to be used as first-aid compound against unforeseen viral epidemics or pandemics.

SARS-CoV-2 is still a major problem for humans, and there are currently no officially approved drugs to treat COVID-19

Now a days, the metallic nanoparticles and dendrimers are most widely used to treat the variousviral infection diseases.

CONCLUSIONS

The above study revealed that nanotechnology has facilitated the production of many highly effective biosensors, Nano vaccines, and antiviral composites for close-related viruses, makingthis compilation a valuable guide to the development of SARS-CoV-2 agents. Therefore, nanotechnology has a lot to give in the fight against the COVID-19 pandemic, and the specialproperties of nanosized sensors, vaccines and antiviral nano Nano sensors will be crucial in thecoming months or year.

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