VOL- VII | ISSUE- VIII | AUGUST | 2020 | PEER REVIEW e-JOURNAL | IMPACT FACTOR 6.293 | ISSN 2349-638x

Application of Nanotechnology in Covid-19

Mr. Digvijay Rajesh Patil
School Of Nanoscience And Technology,
Kolhapur.

Abstract-

The novel corona virus disease reported in Wuhan China in December 31 2019, has affected all the world including India. By August 9 2020 Covid-19 has affected more than 2.09 M people in India.Most important an only way to fight against covid -19 is developing better prevention , diagnosis and antiviral methods which can be possible by using nanotechnology . Nanotechnology as a emerging field in Science is introduced in controlling Covid-19. Nanotechnology is used in manufacturing mask and developing nanocoating which can prevents us from infecting with SARS-CoV-2. Traditional mehods used for testing are not as simple and are also time consuming. But nanoparticles like gold, Titania , Iron Oxide are used in making Testing kits for Covid-19. Laser based testing kit can detect day one infection in patient. Polymeric nanoparticles , Nanospheres , Peptide nanostructures are used in developing nanovaccines which can neutralize SARS-CoV-2. In this paper various upcoming research in combating covid-19 is been outlined.

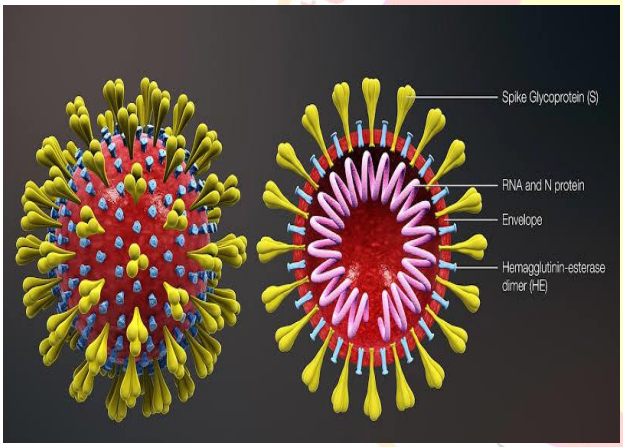

Figure:1 SARS-CoV-2

Introduction-

Coronavirus disease 2019 is an infectious disease caused by a newly discovered severe acute respiratory syndrome coronavirus 2(SARS-CoV-2). Common symptoms include fever, cough, fatigue, shortness of breath, loss of smell and taste. Compared to previously identified severe acute respiratory syndrome and middle east respiratory syndrome fatility rate is low but transmition rate is more. The virions of SARS-CoV-2 are in form of spheres with an average diameter of 125 nm with lipid based viral envelopes and positive sense single stranded RNA genome. Virus consist of four type of structured proteins. Spike(S), Membrane(M), Envelope(E), Nucleocapsid(N) proteins among which S protein has a crucial role in attaching virus to its host cell and then entering cells. Coronaviruses are a large family of viruses that attack upper and lower respiratory tract in human. More than 100 of coronavirus are known of which 7 has been proved to cause human infectious. The four are 229E (alpha coronavirus), OC43(beta coronavirus), NL63(alpha coronavirus), HKU1(beta coronavirus) causes mild diseases. SARS-CoV, MERS-CoV, Covid-19 are very lethal. SARS-CoV-2 is closely related to SARS-Cov. The virus enters host cells through angiotensin-converting enzyme 2 (ACE2) which is present in lungs. Hence,lungs get much affected by SARS-CoV-2. Virus uses Spike protein to bind ACE2 and then enters the host cell. SARS-CoV-2 may cause respiratory failure it can affect brainstem as other corona virus has found to invade central nervous system.

Nanotechnology is manipulation of matter on an atomic, molecular and supramolecular scale. Nanoparticle are particle of matter that is between 1 and 100 nm. As S protein is important an effective way of fighting with virus by targeting S proteins mechanism by developing special drugs and inhibiting compounds. Due to unknown hazards vaccine developed should has a long term safety. Chloroquine used in prophylactic drugs for antimalaria medicines has been reported. Chloroquine used in combination with nanomedicine to visualized cellular uptake and reduce viral replication. Existing vaccines has several downfalls ,

failure to engage immune system to its full effect , low stability in vivo, high toxicity and storage of vaccines to maintain it at optimum temperature until use are important reasons to focus on nanovaccines. Also nanovaccines target directly at site in body which is being infected. In plasma therapy also there are risk. Serum disease which is associated with transmission of blood infection from other person body. And also it is important to identify human monoclonal antibody that neutralizes SARS-CoV-2.

In similar way as in vaccine developing nanotechnology is also used in preventing and diagnosing SARS-CoV-2. Graphene, Graphene Oxide , Titanium Dioxide, Iron Oxide, Gold nanoparticles are used in preventing and diagnosing SARS-CoV-2.

NANOTECHNOLOGY IN PREVENTION AGAINST SARS-CoV-2

1. Reusable Graphene Mask –

Graphene is an allotrophe of carbon consisting of a single layer of atoms arranged in two-dimensional honeycomb lattice. Graphene conducts heat as well electricity along its plane very efficiently. It has outstanding physical,chemical,electrical and mechanical properties. Its high surface area, strength, conductivity makes it special. Researchers has shown that graphene also has antibacterial properties. The nanosized sharp edges of graphene and its atomic composition are reported to contribute antibacterial properties. Researchers has also shown that smaller the size and high the density of attached functional groups to graphene more the antibacterial activity.[2] By considering this renowned properties LIGC Applications Ltd. New York this company has developed a reusable face mask is also named as Guardian G- volt mask which uses both graphene and electrical charge to repel virus. G- volt mask is 99% efficient again 0.3 µm and 80% effective against anything smaller. For comparison N95 respirator mask blocks 95% 0.3 µm virus. Viruses such as coronavirus can be transmitted through tiny droplets of water. A low level of electrical charge will pass through G – volt when it will be plugged in battery through USB port. This charge would repel any particle trapped in mask. At home a docking system will allow mask to be fully sterilized so that it can be worn again. This mask is helpful for those which are in direct contact with virus. Mask protect against virus near mouth and nose region. Graphene used in mask is Laser Induced Graphene(LIG) a microporous conductive foam that can trap bacteria and electricity to sterilize it. [3]Swatantra P. Singh et.al showed that LIG printed on polyamide film is extremely resistant against microbial fouling and exerts anti-microbial action even no external voltage was applied and when external voltage was applied its property enhanced.

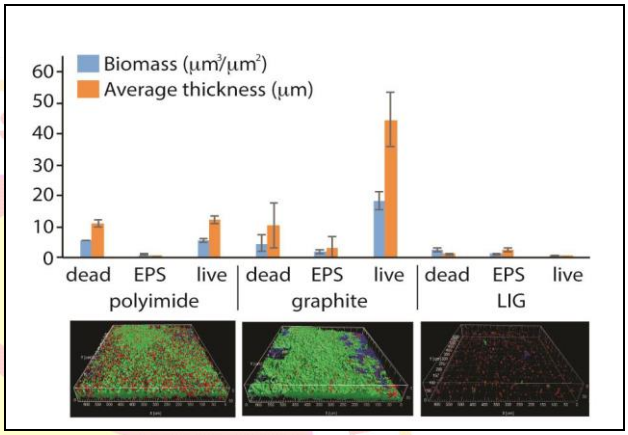

Figure 2: Biofilm growth on the polyimide, graphite, and LIG surfaces with using secondary treated wastewater showing biomass and average thickness. Representative IMARIS software images for polyimide; graphite; and LIG are seen. Green, red, and blue represents live bacteria, dead bacteria, and EPS, respectively. Reprinted from ref.3.

2. Anti- viral activity of Graphene Oxide(GO)-

Loading anti viral agents on Graphene oxide(GO) not only produces antiviral synergistic effect but also enhances biocompatibility and reduces cytotoxicity of drug. Due to their 2-d structure , sharp edges , and negatively charged surfaces GO nanosheets are capable of interacting with viruses and also disrupting their plasma membrane or by generating reactive oxygen species. [4]GO high drug loading capacity and low cytotoxicity make it good choice of drug carrier which is shown by researchers of Sichuan Agricultural University. Both the in vivo and in vitro studies were conducted by loading an optimized dosage of hypericin on G.o. Hypercine is a substance whose antimicrobial properties has been proved

very long years. Research on hypericine has shown that hypericine and its derivatives extracted from Hypercium Perforatum shows antiviral activity against various viruses like chronic hepatitis C virus, Sendai virus,influenza virus herpes simplex virus types 1 and 2 etc. The antiviral combination of G.O and hypericin was tested against novel duck reovirus (NDRV) and reported to inhibit its replication by preventing transcription of its target gene. Furthermore, researchers has found that antivirus nanomedicine designed on G.O which have been tested against various viruses can also show similar kind of antiviral effect against Novel Coronavirus too. [5]Shiyi Ye et.al showed antiviral activity of G.O and reported the broad spectrum antiviral activity of G.O against Pseudorabies virus(PRV, a DNA virus) and Porcine Epidemic Diarrhea Virus (PEDV, a RNA virus). The overall resuly suggest the potential application of G.o as a novel antiviral agent. Ting Du et.al showed that G.O0AgNp nanocomposites could inhibit better than AGNp and G.O. The broad antiviral activity were proved against Porcine Epidemic Diarrhea Virus (PEDV) as a contras virus.

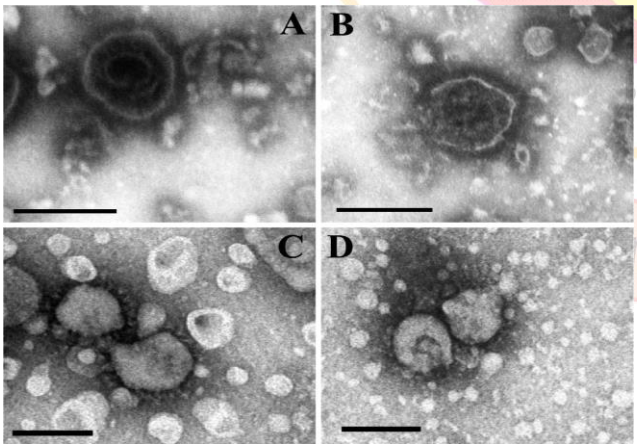

Figure-3 Transmission electron microscopic images of G.O treated viruses, A) PRV Control, B) PRV treated with G.O for 1 hour, C) PEDV control, D) PEDV incubated with G.O for 1 hour, sacle bars: 200 nm (A,B) and 100 nm(C,D). Reprinted from ref.5

3. Titania Based Photocatalytic Nanocoating-

Titanium Dioxide also known as Titania is a naturally occurring oxide of Titanium. FDA of US approved it safe and harmless to human and animal.[7] F N Nano Inc, a USA based company specializing in photocatalytic intelligent multifunctional coating has developed a new photocatalytic nanocoating based on Titanium Dioxide which can decompose and eliminate organic compound , bacteria, viruses etc. It works on oxidative decomposition. It means that if Titanium Dioxide exposed to light organic substances on the surface will be broken down to oxidation eventually forming carbon dioxide and water. A new photocatalytic nanocoating based on titanium dioxide which can decompose and eliminate organic compounds, viruses, bacteria, on its surface when exposed to light and hence coronavirus . The spread of Novel Coronavirus thus can be prevented in hospitals , government building and public places.[8] Han, W et. al showed that Photocatalytic Titanium Apatie Filters (PTAF) material could inactivate SARS-CoV virus suggesting us that Titanium based material can also prevent us from SARS-CoV-2 as SARS-CoV-2 shares up to 80% genome with SARS-Cov. The inactivation of SARS-CoV by PTAF was tested and it showed upto 99.99% inactivation after 6 hour interaction under non-ultraviolet irradiation. [9]Foster et. al showed in the review the overview effect of photoactivated Titanium Dioxide on microrganism , fungi, algae and mammalian viruses. The kiling mechanism involves degradation of Cell wall and cytoplasmic membrane due to production of Reactive Oxygen Species. In Table 1 The Viruses that have been killed by Photocatalytic degradation using Titanium Dioxide are shown. Norovirus belong to family Calciviridae and are grouped of non enveloped single stranded RNA viruses that primarily causes acute gastroenteritis (Inflammation of Stomach).[10] Kato et. al demonstrated the degradation of Norovirus in Sewage Treatment water by a combined photocatalytic/ UV disinfection (Titanium Dioxide/UV) system. Titanium dioxide and UV system was effective in decomposing Norovirus particles and reducing its concentration in sewage effluent.

Serial Number	Host	Viruses
1	Birds	Influenza (avian) A1H5N2
2	E- coli	Coliphage
3	Human	Norovirus
4	Human	Poliovirus type 1
5	Human	Severe Acute Respiratory Syndrome Corona Virus.

Table no-1 Viruses that has been neutralized by PCD using Titanium Dioxide. Reprinted from ref. 9

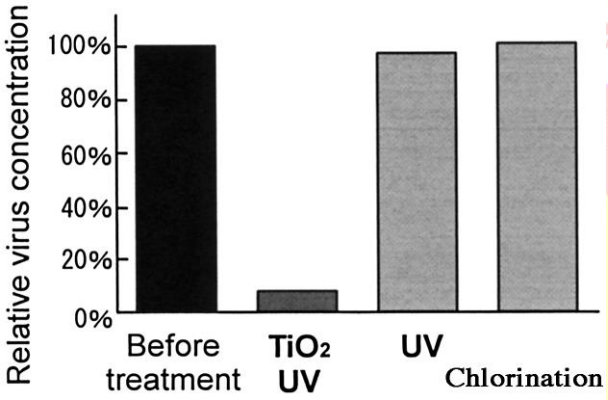

Figure – 4 Comparison of decomposing efficacy of TiO_2/UV, UV , Chlorination. Reprinted from ref. 10.

NANOTECHNOLOGY IN DIAGNOSIS OF COVID-19

1. Laser Based Instant Corona Test-

European photonics scientists are developing an ultrasensitive laser sensor that detects corona virus at earlier stage of infection from a saliva or nasal swab that can detect virus in minutes(Optical Biosensor). It has ability to diagnose in real time with very low concentration of sample. Using photonics technology that manipulates light ultrasensitive demonstrator could detect day 1 infection in patients who have low viral load. Looking at tiny molecules new point of care detector examines virus antigens using miniaturized chips or nanophotonic biosensor from a simple nasal or saliva swab. Once sample is prepared and is place device conforms positive or negative for coronavirus, procedure is of 30 minute. Nanosensor is capable of detecting RNA strands which fully identify novel coronavirus. The bioreceptors on sensor surface are tuned to a particular antigen of virus,only coronavirus molecule is captured. Sensor works on interferometric technology, as the virus molecules bind to sensor surface sensor produces a new signal when virus is present. A nano interferometric Biosensor are most sensitive label free detection technology. Light travelling in sensor generates evanescent field of few nms over sensor surface. Here receptors can recognize antigens of virus capsid when a respiratory fluid sample passes through it. This recognition event causes change in refractive index due to which light slightly changes its direction of travel. This change can be measured. CONVAT team, coordinated at Catalan Institute of Nanoscience and Nanotechnology, Spain (ICN2) researchers have tested on patients sample provided by Vall D' Hebron Hospital in Barcelona and several hospital in Spain. Photonics is renowned for its rapid and clean detection hence it can be a perfect device to detect Novel Corona virus.

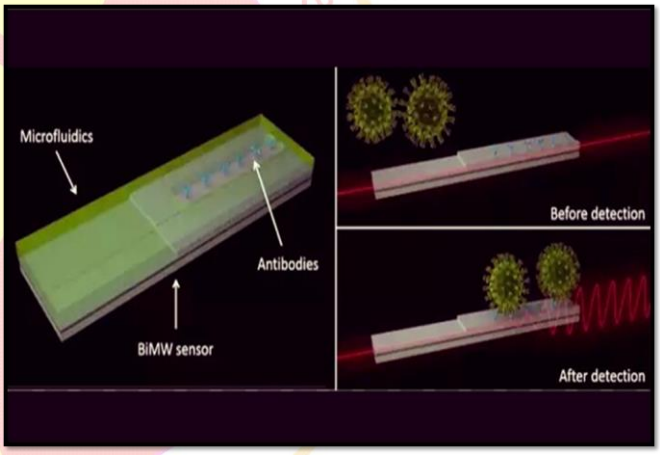

Figure-5 Working of Laser Based Instant detection device. Reprinted from ref. 11.

2. Silica Coated Iron Oxide Nanoparticles(NPs)-

Silicon dioxide also known as silica is an oxide of Silicon. [11] Researchers at NTNU's Department of Clinical and Molecular Medicine and Department Of Chemical Engineering in collaboration with St. Olav's Hospital are developing a method for diagnosis of novel corona virus that uses magnetic nanoparticles.Tiny iron oxide NPs coated with silica may seem like an unlikely player in enabling Norway to fight corona virus. Around 1,50,000 test are done per week. It turns out that iron oxide Nps coated with silica have a strong affinity for RNA genetic material inside virus causing covid - 19. New test uses Nps to extract RNA from a solution containing a sample from patient. The solution contains substances that crack virus open so that its genetic material can be extracted. RNA from virus attracted to silica covered magnetic NPs. The

next step is to use a magnet to pull RNA covered particles out of solution. We can identify genetic code from RNA and compare it to novel corona virus.[12] Yang et. al showed A rapid Silica Spin Column – based method of RNA extraction from Fruit trees for RT-PCR detection of viruses. In presence of chaotropic salts the adsorption of nucleic acids to surface of glass or silica was first described by Vogelstein and Gillespie. Now in present selective binding of DNA or RNA has been achieved through use of modified silica gel surfaces and binding and wash buffers have also been optimized to allow maximum discrimination between nucleic acids. In the process of silica gel surfaces for nucleic acid extraction as soon as lysis of starting material is done the sample is adjusted to specific binding for desired nucleic acids to membrane. The proteins and polysaccharides are removed which do not bind. The bounded DNA or RNA are then washed with alcohol containing buffer for desalting. Pure DNA or RNA are then eluted in water or low salt buffer.(Shown in fig.6) This method which is reported can give us idea that Silica is good option for RNA extraction and is biocompatible.[13] Alex H et. al prepared Iron Oxide Silica nanoparticles for Zika Viral RNA extraction. In this paper a novel way for preparing Silica coated Iron Oxide particles are presented and its application in extracting Zika Viral RNA from the serum followed by a PCR based assay. Similar way can be achieved in extracting RNA of Novel Corona virus from the given sample.

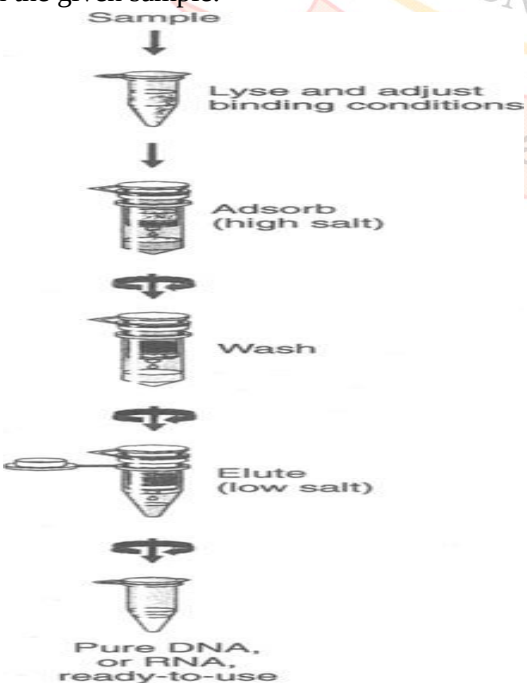

Fig- 6 General procedures for Isolation of DNA or RNA using Silica Gel based membranes in spin columns. Reprinted from ref.12

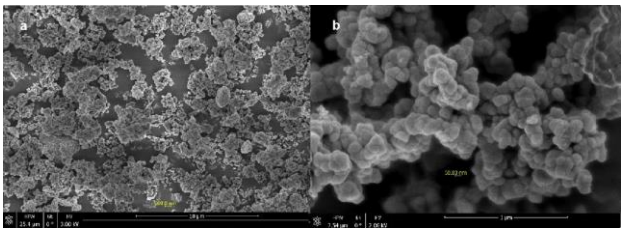

Fig- 7 (a) SEM analysis of Fe3O4@Silica with 500 nm & 10 mm scales.
(b) SEM analysis of Fe3O4@-Silica with 50 nm & 1 mm scales
Reprinted from ref.13

3. Rapid Nano Gold based test kit-

[16] The unique properties of gold Np their rich surface chemistry and low toxicity as well as easy method to synthesis has promoted its application in diagnosis, vaccine development, drug carrier etc. [15] All are relying on true polymerase chain reaction, Uk companies researched on antibody test kits for use as rapid diagnostic tools for novel corona virus. The antibody tests use Au Nps in test strip that detect covid-19. As a sample in this case a blood sample from a finger prick is used . Blood moves along strip biomarkers come in contact with antibodies and causes a colour change . Ionic interaction takes place between positively charged group in antibodies and negatively charged surface of Au Np.No need of a professional doctor anyone can do as it is simple and easy. The antibody test are able to detect infection where patients may be asymptomatic or where PCR tests may give false or negative results. Detect both IgM a generalized infection biomarker and IgG a more specific SARS-Cov-2. IgG antibodies developes in patient within 10 days after symptoms of Covid-19 begin. And IgM antibody are first antibody produced by immune system when a virus attacks. The accuracy of Nano gold test kit is upto 99.6% respectively.

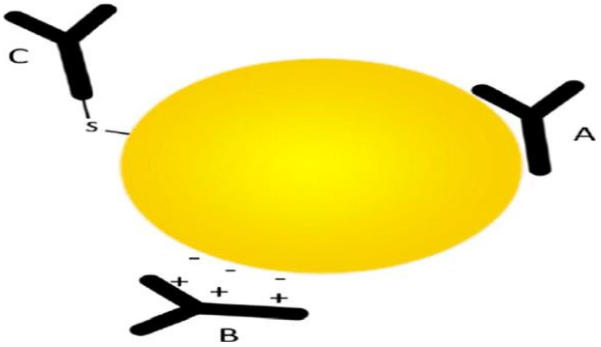

Fig-8 Hydrophobic and Ionic Interaction between Antibody and Gold nanoparticle surface
A) Hydrophobic interaction B) Ionic Interaction C) Covalent bond is formed due to dative binding. Reprinted from ref.16

NANOTECHNOLOGY IN DEVELOPING VACCINE

1. **Novavax Formulates Covid-19 vaccine-**

[17] NVX-CoV2373 a stable prefusion protein made using Novavax propeitary Np technology. [18]Purified NVX-CoV2373 S form 27.2 nm Nps that are thermostable and bind with high affinity to human angiotensin converting-enzyme2. Novavax Propeitary Matrix-M adjuvant will be incorporated with NVX-CoV2373 in order to enhance immune response and stimulate high levels of neutralizing antibodies. NVX-CoV 2373 has shown to be highly immunogenic in mice and baboon measuring spike proteins specific antibodies antibodies that block binding of spike protein to receptor and wild type virus neutralizing antibodies. High spike protein specific antibodies with human angiotensin converting enzyme 2 in human receptor binding blocking activity was seen and SARS-CoV-2 neutralizing.

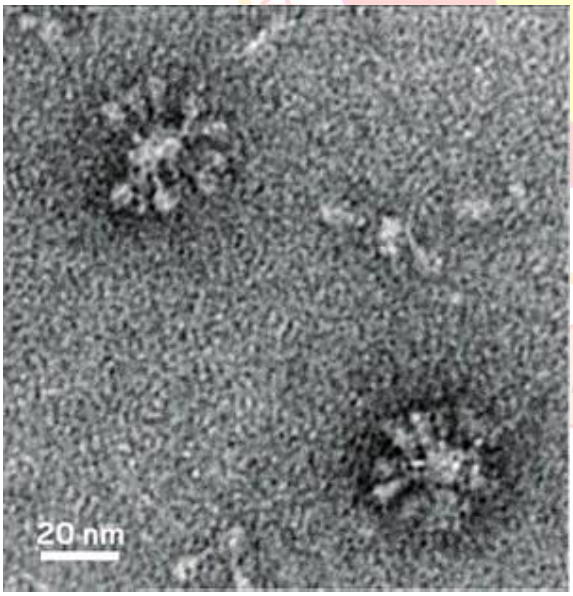

Figure- 9 An Electron Microscopic Image showing nanoparticles of the respiratory syncytial virus(RSV) F protein in Novavax RSV Vaccine. The firm will make a similar Nps with SARS-CoV-2 spike proteins for its vaccine. Reprinted from ref.17.

2. Moderna Lab-

[19]mRNA vaccine (mRNA-1273) against SARS-CoV-2 phase 1 study conducted. mRNA -1273 lipid nanoparticle dispersion containing an mRNA that encodes for prefusion of the stabilized S-protein in virus structure. mRNA-1273 consist of mRNA Drug substance that is placed inside of Lipid Nanoparticles. Lipid Nanoparticles are composed of cholestereol, commercially available lipids and propeitary ionizable lipids.[21] In phase 1 study 45 Healthy adults in age groups from 18-55 years were chosen and dose escalation were done. They received two vaccination 28 days apart in a dose of 25µg,100gµ or 250µg. There were three groups based on dose group containing 15 participants each. Antibody responses were higher with higher dose were seen after first vaccination was completed.(day 29 GMT, 40,227 in 25µg group, 109,209 in 100µg and 213,526 in 250µg group). Titers increased after second vaccination. Fatigue,Chills,headache,myalgia and pain in the injected site were solicited adverse effects that occurred in more than half the participants. After second vaccination systematic adverse effects were more common specially with highesr dose group and 3 partcipants (21%) in 250µg dose group reported to have one or more severe adverse effect. The mRNA-1273 vaccine shown good immune responses in all the participants. [20]This approach is breathtaking as no mRNA vaccine has been licensed yet in any other infectious disease. After completion of phase 2 trail Moderna has aplan for Phase 3 trail. Its planned to enrolled 30,000 partcipants around 27 July 2020 as a start date. However, the confirmation of vaccine requires large clinical efficacy study.

Characteristic	25-µg Group (N=15)	100-µg Group (N=15)	250-µg Group (N=15)	Overall (N=45)
Sex-no. (%)				
Male	9(60)	7(47)	6(40)	22(49)
Female	6(40)	8(53)	9(60)	25(51)
Age-yr	36.7±7.9	31.3±8.7	31.0±8.0	33.0±8.5
Race or ethnic group-no.(%)				
American Indian or Alaska Native	0	1(7)	0	1(2)

Asian	0	0	1(7)	1(2)
Black	0	2(13)	0	2(4)
White	15(100)	11(73)	14(93)	40(89)
Unknown	0	1(7)	0	1(2)
Hispanic or Latino no.(%)	1(7)	3(20)	2(13)	6(13)
Body Mass Index	24.6±3.4	26.7±2.6	24.7±3.1	25.5±3.2

Table.no-2 Characteristics of the participants in the mRNA-1273 trial enrollment. Reprinted from ref.21

3. Chloroquine-

A chloroquine is a 70 year old medicine it primarily used to combat Malaria. It was further used to investigation of nanoparticle uptake in cells and showed a possibility in developing an effective treatment to SARS-Cov-2. Chloroquine and its derivative has a long history as a safe and inexpensive drugs for treatment of some autoimmune disease. Cell culture has showed that Chloroquine has antiviral activity against SARS-CoV and OC43 it is hypothesized that mechanism involves inhinition of viral fusion and prevention of host receptor protein glycosylation. Chloroquine has been demonstrated to be an effective inhibitor of Np endocytosis. [22]Furthermore it has proved it reduces expression of Phosphatidylinositol binding clathrin assembly protein(PICALM) which plays a vital rele in the rate of endocytosis. The deficiency of PICALM leads to inhibition of clatharin mediated endocytosis. Chloroquine is a weak base that can enter membrane. SARS-CoV-2 is spherical 140nm it may enter cells through clatherin mediated endocytosis which may be hindered by chloroquine due to PICALM suppression. For entering cells virion needs S protein to be cleved with endosomal proteases and undergo conformational change. Endosomal Protease like Cathepsin are activated by acidification of endosome, thus chloroquine increasing pH of endosme can affect whole process and prevent virus entering cells. [23]But also caution should be taken while while assessing Chloroquine as its higher dose can cardiac arrest and even kidney injury may occur. Initially Cardiac evaluation should be done of patients. Twice in a week residual blood concentration monitoring should be done of a hospitalized patients.

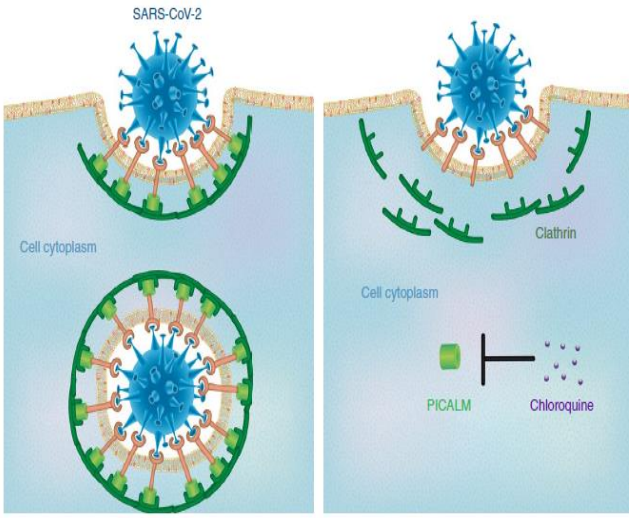

Fig: 10 Mechanism of Chroquine against Covid-19. Reprinted from ref.24.

Conclusion-

In this appraisal, the existing advancement in neutralizing Covid-19 with nanotechnology has been summarized. The studies concerning the prevention , diagnosis, and vaccine development as a present scenario has been pondered upon. Nanotechnology has been exploring in Covid-19 neutralizing due to its quantum confinement effect, large surface to volume ratio and edge effects etc. A short review of some industries developing vaccine are been presented with some statistical data. However, the investigation in developing a perfect and unbeatable vaccine requires further efficacy studies. Nevertheless , nanotechnology have shown many distinct advantages and great potential to replace some traditional materials for combating Novel Corona virus.

References

1. www.wikipedia.in
2. www.Statnano.com ; Reusable Graphene Mask Sterilises Itself against Coronavirus with Electrical Charge.
3. Laser Induced Graphene Layers and Electrodes Prevents Microbial Fouling and Exerts Antimicrobial Action; Swatantra P. Singh, Yilun Li, Avraham Be'er, Yoram Oren, James M.Tour and Christopher J. Arnusch; ACS Applied Materials And Interfaces 2017 9(21), 18238-1827 DOI: 10.1021/acsami.7b04863.
4. www.Statnano.com; Synergistic Antiviral Activity of Graphene Oxide and Common Antiviral Agents.

5. Antiviral activity of G.O : How sharp edged structure and Charge Matter; Shiyi Ye,Kang Shao,Zhon ghua Li, Nan Gua,Yunpeng Zuo,Qin Li, Zhincheng Lu,Lu chen,Digui He and Heyou Han ACS Applied Materials and Interfaces 2015 7(38),21571-21579: DOI: 10.1021/acsami.5b06876
6. Antiviral activity of Graphene Oxide- Silver Nanocomposites by preventing Viral entry and activation of the Antiviral Innate Immune Response; Ting Du, Jian Lu, Lingzhi Liu, Nan Dong, Liurong Fang, Shaoba Xiao and Heyou Han; ACS Applied Biomaterials 2018 1(5), 1286; DOI: 10.1021/acsabm.8boo154.
7. www.Statnano.com, Titania-based Photocatalytic Nanocoating, First Line of Defense Against Coronavirus.
8. Han,W and Zhang , P-H and Cao, Wi- Chun and Yang, DL and Taira, S and okamoto, Y and Aral, J-I and Yan, Xiyun(2004). The inactivation effect of photocatalytic titanium apatie filter on SARS virus. Progress in Biochemistry and Biophysics 31.982-985.
9. Foster , Howard and Ditta, Iram and Varghese , Sajnu ans Steele , Alex (2011). Photocatalytic disinfection using titanium dioxide : Spectrum and Mechanism of Antimicrobial activity. Applied Microbiology and Biotechnology. 90.1847-68.10.1007/s00253- 011-3213-7.
10. Kato , Toshiaki and Shibata, Toshiyuki and Tohma, Hisao and Tamura,Motonori and Miki, Osamu.(2005) Degradation of Norovirus in Sewage Treatment Water by Photocatalytic Ultraviolet Disinfection. Nippon Steel Technical Report.
11. www.Statnano.com, Photonics Scientists develop Laser Based Instant Saliva Test for Corona Virus.
12. Yang, Fan, Wang, Guoping , Xu , Wenxing. Hong, Ni, A rapid Silica spin column based method of RNA extraction from fruit trees for RT-PCR detection of viruses- Journal of Virology methods https://dx.doi.org/10.1016/j.viromet.2017.05.020
13. Alex H, F. Lee, Steven F. Gessert, Yutao Chen , Nikolay V. seergeev, Bubak Haghiri. Preparation of iron oxide silica particles for Zika viral RNA extraction. Heliyon 4(2018)e00572. doi: 10.1016/j.heliyon.2018.e00572.
14. www.Statnano.com, Silica Coated Iron Oxide Np in Covid-19.
15. www.Statnano.com, Rapid nano gold Corona virus test.
16. Mir Hadi Jazayeri, Hamed Amani, Ali Akbar Pourfatollah, Hamidreza Pazoki- Toroudi, Bijun Sedighimoghaddum. Various methods of gold nanoparticles conjugation to antibodies. https://doi.org/10.1016/j.sbsr.2016.04.002
17. www.Statnano.com, Novavax's First in Human Coronavirus vaccine is set to be tested in mid-may.
18. www.Novavax.com, SARS-CoV2 spike glycoprotein vaccine candidate NVX- CoV 2373 elicits immugenecity in baboon and and protection in mice.
19. www.Statnano.com, Moderna Runs First Human Trial for Corona Virus vaccine.
20. www.Statnano.com, Moderna Starts Phase 3 Trail of corona virus vaccine – But its Promise Is still unclear.
21. The New England Journal of Medicine; An mRNA vaccine against SARS-CoV-2- Preliminary Report; L.A Jackson, E.J Anderson, N.G Rouphael, P.C. Roberts, M. Makhene, R.N Coler, M.P Mccullough, J.D Chappel, M.R Denison, L.J Stevens, A.J Pruijssers, A. McDermott, B.Floch,N.A Doria Rose, K.S. Corbett, K.M. Morabito, S.O'Dell, S.D Schmidt, P.A. Swanson II, M.Pdilla, J.R. Mascola, K.M Neuzil, H.Bennet,W.Son,E.Peters, M. Makowski, J.Albert,K. Cross , W Buchanan, R. Pikaart- Tautges, J.E.Ledgerwood, B.S. Graham and J.H. Beigel for the mRNA-1273 Study group.
22. www.Statnano.com, Heres how nanomedicine provides insights into chloroquine efficacy against Covid-19.
23. Bruno Megarbane (2020): Chloroquine and hydroxychloroquine to treat Covid-19 between hope and caution, Clinical Toxicology, DOI: 10.1080/15563650.2020.1748194.
24. Tony Y. Hu, Matthew Frieman and Toy Wolfram; Insights from nanomedicine into chloroquine efficacy against Covid-19.