

# Eminent role of Nanotechnology in Detection, Diagnosis and treatment to Combat COVID-19

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## *Abstract*

*Today world is facing huge challenge to combat spread and death cause due to novel corona virus (COVID-19). This infectious disease cause tremendous amount of damage to human population medically as well as economically. COVID -19 also affected badly on education worldwide. Until date, no evident treatment or vaccine has been suggested for the treatment of COVID-19. Doctors are using different combination of antiviral medicines. They also using plasma therapy. The only way to prevent oneself is to maintain social distancing, proper hygiene and wear mask. Nanotechnology can play very important role in combating COVID-19. Nanoparticle can be used in Nanomedicine. It can also coat or spray on mask or PPE kit for protection. It has also used for early detection of Covid 19 patients. The present paper aim to present comprehensive role of nanotechnology in curbing menace of SARS-CoV-2. The paper will also present different chemical route for synthesis of nanoparticles, which is being or would be used for limiting the risk of Covid 19.*

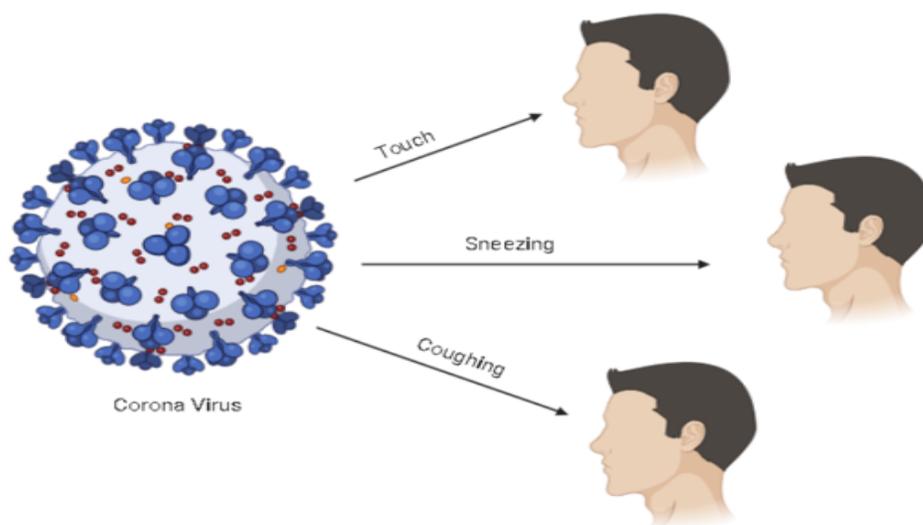
*Key words: COVID-19; nanotechnology; nanoparticle; Drug; Chemical method; Microemulsion*

## **Introduction**

The world has witnessed one of the most deadly pandemic affecting almost majority of the countries in the world in the year 2020. This disease outbreak started from a local seafood market in Wuhan, Hubei province, central china. The full length genome sequence obtained from some patients were found identical to SARS –CoV and the 2019-ncov is 98% identical at the whole genome level to a bat coronavirus. [1]. The world health organization has recognized this pathogen as a coronavirus disease (Covid 19) on February 11, 2020 and the International Virus Classification Commission has designated the novel coronavirus as Severe acute respiratory syndrome Corona virus 2 (SARS CoV-2) [2]. The WHO has announced Covid 19 as the Public health emergency of international concern (PHEIC) on 30 January 2020 [3] and a pandemic on 11

March.(4).In the past two decades, two large scale pandemics ,SARS and MERS have already been caused by coronaviruses{5,6} SARS -CoV-2 has emerged as a highly pathogenic coronavirus into the human population. Global coronavirus cases have surged to 80.4 million with deaths approaching 1.76 million and approximately 45.5 million people have recovered on 26 December 2020. (7)

The virus spreads through close contact via small droplets produced by coughing, sneezing and talking (**figure 1**). It can also spread through touch of contaminated surface and then touching the eyes, nose and mouth {8}. There is no evident vaccine and medicine for the treatment of COVID-19. World have used different combination of medicine to treat COVID-19. USA has used hydroxychloroquine and remdesivir. In India doctors used Lopinavir and Ritonavir with Oseltamivir and chloroquine. Few patients have also administered swine flu medicine Tamiflu.

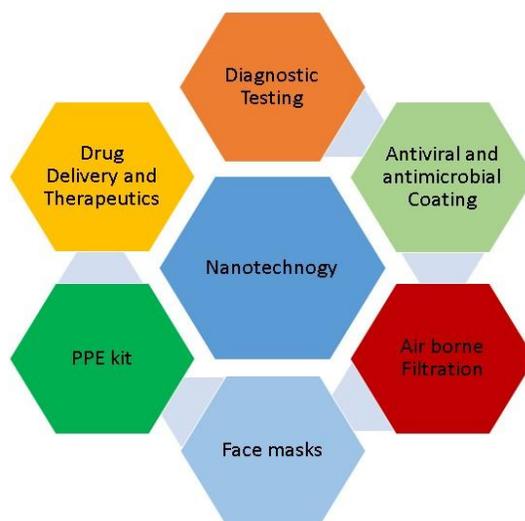


**Figure 1: Spread of corona virus**

China has given COVID-19 patients anti HIV drug Lopinavir or Arbidor. They have also used Favilavir and Favipiravir. Russia is giving antiviral drug Avifavir. Many more countries administered different type of antiviral and anti HIV drug to their patients (9). No medicine is so effective in treating this deadly disease. Therefore, our most significant defense is our immune system. But people who are suffering from co-morbidity like heart disease, kidney disease, liver ailment, diabetes etc or who are immunocompromised are at high risk of getting infection. Scientists are doing research round the clock to get something new medicine or vaccine that would be effective against the deadly virus, but nothing substantial achieved. Hence we can say that nanotechnology and nanoscience may play very vital role in minimizing the jeopardy of life around the world. Nanotechnology is considered as the impending technology of 21st century and is envisaged as a big godsend in the medical science. The term nanotechnology is the combination of two words: namely, technology and the Greek numerical “nano” which means

dwarf. Thus, nanotechnology is considered as the science and technology used to develop or manipulate the particles in the size range of 1 to 100 nm (10, 11). Nanobiotechnology is the interface between nanoscience and biotechnology, which concomitant area known as nanomedicine that covenants with the solicitation of nanostructured materials to diagnose, treat, and avoid diseases.

The first nanotechnology applied in medicine were presented to increase the efficiency of current, yet dose-limiting and poorly bioavailable drugs (15) presently, There are various mechanism are acknowledged to employ antiviral activities of nanoparticle. First, the distinctive physical and chemical properties of nanoparticles such as (1) small particle size (which can expedite drug delivery into structurally advantaged locates) (16, 17) (2) large surface area to volume ratios (which guarantees the billetion of the large drug payloads), (18) and (3) tunable surface charge (which is to enable cellular entry across the negatively charged cellular membrane), (19, 20) make nanoparticles attractive tools for viral treatment. Second, nanoparticles can have biomimetic properties, (21–23) which consequence in inherent antiviral properties. Widespread examples of these comprise silver nanoparticles (24, 25) and dendrimers. (26, 27). In addition, because of protective properties of nano material, it can make a defensive layer, which prevent the degradation of encapsulated medicine or anti infection agent. (28,29). To combat SARS-CoV-2, Nanotechnology and nanoscience can be used in many way like in diagnostic kit, antiviral and antimicrobial coating, air borne filtration, Facemask, PPE kit, drug delivery and Therapeutics (**Figure 2**)



**Figure 2: Application of nanotechnology in combating Covid 19**  
**Coating or Spraying of PPE kit and Face masks**

Coating of masks and PPE kits with nanomaterial, that will be antiviral in nature, may be useful in protection from the COVID 19. When the virus touches the surface, the nanoparticle present on the surface of PPE kits and facemasks interacts with virus, it automatically get destroyed and surface will become safe. Some of nanomaterial has antiviral and anti-microbial properties. Like copper, Silver and gold nanoparticle. Copper is cheaper so it will be easily affordable by all type of citizens. So copper nanoparticle along with polymer would be a very useful for coating (30)

### **Airborne Virus filtration**

As The deadly disease, COVID 19 spread through sneezing, coughing and talking. Therefore, virus will transmits through air. So nanoparticle of cellulosic fibre can be a fantastic material for increasing the efficiency of normal medical mask just by coating of nanocellulosic fibre(31) Nano TiO<sub>2</sub>.may be a landmark infiltration of air borne virus(COVID 19). Nano TiO<sub>2</sub>.is a semiconductor. Semiconductor is that material which has energy gap between valence band and conduction band. Hence it absorbs energy excitation of electron takes place from valence band to conduction band. Therefore, due to decrease in size energy of band gap increases hence it can absorb UV, which can can destroy the SARS Virus. Coating of nano silver can also be helpful in restricting the spread of virus because silver has also antiviral possessions

### **Diagnostic Testing**

Scientist from University of Maryland School of medicine made a diagnostic kit for detecting Corona virus in just 10 minutes. They have used Gold nanoparticle for developing kit. RNA is extracted form nasal swab and dipped into the solution which contain Gold nanoparticle. A specific molecule attached to the gold nanoparticle to detect a particular protein, which is genomic sequence of Corona virus. The gold nanoparticle solution will turn purple to blue when it interact with Corona Virus (32) **Figure 3**. Some scientist also developed nano gold kit based on IgM/IgE antibody. It take only 15 minutes to screen the Covid patient. (33) Nano silver-based kit can also be developed because it is also antiviral.

Magnetic nanoparticle Iron oxide is also being used in diagnosis of SARS virus. Iron oxide is known for its antimicrobial properties (34, 35) Norway used Iron Oxide coated with Silica based kit to limit the risk of health hazard due to COVID 19. This nanoparticle shows strong affinity towards RNA, the genetic material inside the virus which cause COVID 19.This test practices magnetic nanoparticle to extract RNA from a solution which have a sample of patients. The solution helps in extracting RNA from virus and it attracted towards silica coated iron oxide nanoparticle. Lastly, magnet used to pull out RNA from solution and genetic sequence matched with sequence of corona virus to accomplish the result. Zinc ferrite nanoparticle can also be used for developing such diagnostic kit because it is biocompatible.(36) Graphene and Graphene derived (Graphene oxide), reduced Graphene oxide(rGO) and graphene quantum dots have both antimicrobial and antiviral properties due to movement of electron towards the bacteria.(37-42)

This migration causes cytoplasmic efflux, declines metabolism, affects lipid membrane, prompts oxidative stress, produces reactive oxygen species (ROS), damage of glutathione, and finally

causes bacterial death. It has been itemized that due to hydrogen bonding and electrostatic interaction the lipid bilayer of feline coronavirus adsorbed on graphene oxide and reduced graphene oxide. Graphene oxide has maximum negative charge density and hence it has strong affinity towards positively charged virus. This affinity has been used to developed diagnostic kit for combating havoc of Corona virus (43-48)



**Figure 3: Nasal swab containing Corona Virus**

### Drug Delivery and Therapeutics

As Corona virus create havoc globally by infecting and killing millions of people and there is no evident diagnosis for that, one has to keep social distancing, face cover with mask and maintain good hygiene , which not a permanent remedy to combat this deadly and highly infectious disease. Therefore, it become very important role of nanotechnology in drug delivery and Therapeutics, which can kill Corona virus. **(Figure 4)**



**Figure 4: Killing of Corona Virus**

One medicine Novochizol™ developed by Bioavanta-Bosti. An ideal intra-pulmonary drug release, which could produce nanoparticles, has developed by two-step activation of chitosan and potential Covid-19 active ingredient. Therefore, the active substances could be unconfined

locally, which constrain the inflammatory reaction and avert damage to lung tissue (49). Many more medicine can be synthesized Nano-Silver based, Graphene oxide based in combination with active ingredient. Lot of work need to be done in case of involvement of nanomaterial in developing the drug.

Combination drug therapy is another possibility for treatment of COVID-19, present several benefits such as lower dosages of the individual drugs causing fewer side effects, achieving multiple and complimenting therapeutic targets, and reducing the likelihood of resistance development. Nanocarriers are also essentially very beneficial for the transport of multiple drugs with different physicochemical belongings capable the full prospective of combination healings. (50,51) Different nanomaterials offered flexibility hence production techniques permits the design of drug combinations loaded in Nano carriers with exceptional regulator in conserving synergistic drug ratios, overlapping pharmacokinetics, and reducing combination allied side-effects.(52)

Vaccine is very important medication, which lower the risk of getting pathogenic infection up to good extent by strengthening the immune system. As per record 160 vaccine is under development around the world. 23 of them in clinical trials and 6 in final stages of clinical trial. (53)

Viruses are as small as nanoparticle and therefore it can be viewed as naturally occurring nanomaterials and LAVs (Live-attenuated vaccines), IVs (inactivated vaccine) and viral vectors are nanotechnologies. Being small in size Viruses, it and nanoparticles work at the same length scale; that is why approaches of nanotechnology in vaccine advance and immunoengineering so powerful. The structural features of viruses copycat natural or synthetic nanoparticle however, chemical biology, biotechnology and nanochemistry qualifies the progress of next-generation designer vaccine technologies.

#### **Antiviral and antimicrobial coating**

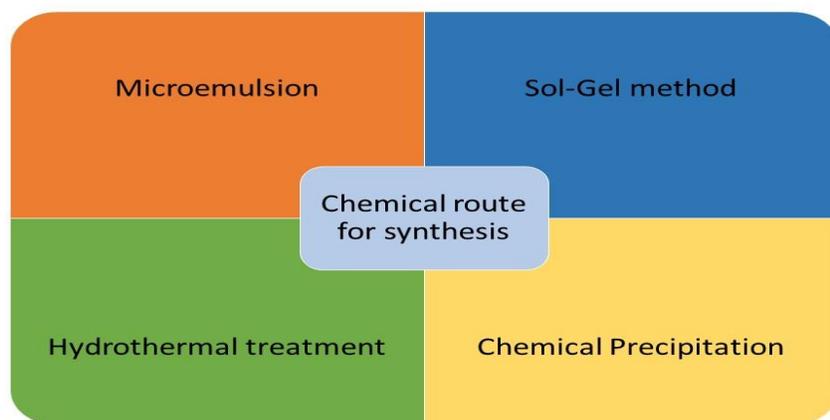
Although Viruses do not grow on non-living surfaces. However, recent studies show that Corona virus remain infectious on many surface such as wood, metal, plastics and fabrics for many hours to days irrespective of surface dirty or clean. However, Corona virus can be easily killed by the solution of ethanol, Hydrogen peroxide or Sodium hypochlorite. But it is not possible to clean the surface all the time and cleaning of surface doesn't guarantee that it will not contaminate again. So it is wise to coat surface by some chemical which repel the pathogens making it nonstick. Glycoprotein of Covid 19 allows virus to get into and bind to ACE2 surface proteins of epithelial cell in respiratory track. Thus surface coating of such material which repel the glycoprotein. Scientist has developed an anti-microbial coating by using Silver nanoparticle as bioactive compound and binder polymers. (54)

Researchers at the Hong Kong University has developed an antiviral that when sprayed onto the surfaces could provide significant protection against SARS-CoV-2. The compound made by using multilevel antimicrobial polymer which contains millions of nano-capsule which formed by heat sensitive polymers that contains disinfectant (55)

Many more nanomaterial can be used for coating which is antiviral and anti-microbial in nature.

### Synthesis of Nanoparticle/Nanomaterial

As we have discussed, role of nanotechnology in lowering the risk of Corona Virus. Various nanoparticle or nanomaterial used in different aspect of medical fields or being used. So synthesis of such nanomaterial with desired properties is very essential. There are different type of methods for the synthesis such as physical method, Chemical method and biological method. Physical method like inert gas condensation, Laser pyrolysis, Physical vapor deposition, melt mixing etc. Chemical method such as micro emulsion, Sol-gel technique, hydrothermal, polyol synthesis. But we will discuss chemical method for synthesis.(figure 5)



**Figure 5: Chemical route for synthesis**

#### Microemulsion:

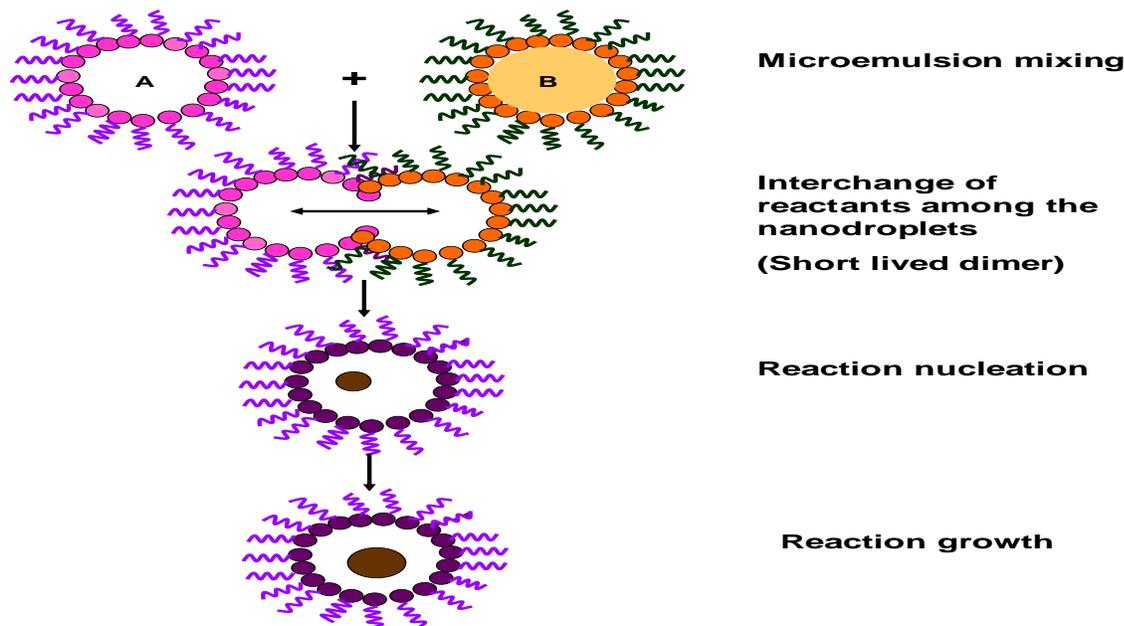
In 1943, Hoar and Schulman first described a transparent system, which formed spontaneously upon the mixing of oil and water with a relatively large amount of ionic surfactant, together with a co-surfactant. The notation “micro emulsion” for these systems was introduced in 1959 by the same authors. They have made quaternary system using benzene, water, surfactant and hexanol. Initially System was translucent but as soon as small chain alcohol added, solution became clear. Micro emulsion is thermodynamically stable and isotropic. There is 3 types of microemulsion (1) Water in oil microemulsion (2) Oil in water microemulsion (3) Bicontinuous microemulsion Different type of nanoparticle can be synthesized using microemulsion method. In this method, As shown in (Fig. 6) two separate microemulsions, which are prepared by dissolving two reactants A and B in the aqueous nanodroplets are mixed. This method bank on on fusion-fission actions between the nanodroplets. The intermicellar collisions and adequately energetic collisions lead to a mixing of miceller insides due to the Brownian motion. The chemical reaction starts only there is perquisite of mixing and when there are fusion-fission event between the droplets. The critical number of molecules is produced after the chemical has taken place between the nano droplets. These outcomes in nuclei formation and additionally tips to the growth of nanoparticles. The micelles endure several collisions and in that way the reactants are swapped, mixed, and react to form the product. Nanoparticles of different materials have been

prepared using this technique. In micro emulsion the size of synthesized nanoparticle are monodisperse.

Using micro emulsion technique different type metal nanoparticle has been synthesized.

Ag has synthesized Ag and Cu nanoparticle and Cu salts of AOT (56). Au and Ag metal nanoparticle obtained by reducing  $\text{HAuCl}_4$  with citric acid at  $80^\circ\text{C}$  (57). Nanoparticles of other metals such as Co, Ni and metal alloys Fe–Ni, Cu–Au and Co–Ni have also been produced using reverse microemulsion (58). Nanoparticles of metal oxide such as  $\text{ZrO}_2$ ,  $\text{TiO}_2$ ,  $\text{SiO}_2$ ,  $\text{GeO}_2$  and  $\text{Fe}_2\text{O}_3$  have been synthesized.(59-62)

Magnetic ferrite nanoparticles such as ternary and quaternary such as  $\text{Ni}_{0.5}\text{Zn}_{0.5}\text{Fe}_2\text{O}_4$ ,  $\text{Co}_{0.5}\text{Zn}_{0.5}\text{Fe}_2\text{O}_4$ ,  $\text{ZnFe}_2\text{O}_4$ ,  $\text{NiFe}_2\text{O}_4$  and many with different stoichiometric coefficient have been synthesized by microemulsion method (63-65). Microemulsion is very facile and economical method for synthesis of any nanomaterial, which can be tailored, for application in medical field to combat SARS-CoV-2



**Figure 6: Schematic of a collision between two reverse micelles with dissimilar cores. The micelles form a short-lived dimer, as some surfactant molecules are released into the oil phase and the contents of the micellar cores are exchanged**

### **Chemical Precipitation/Co-precipitation**

Chemical precipitation/co-precipitation reactions display the following features: (i) The products formed under high supersaturation conditions by precipitation reactions are commonly frugally soluble species,(ii) Such conditions diktat that nucleation is a vital step of the precipitation process and that a large number of small particles will be formed, (iii) Secondary processes, like

Ostwald ripening and aggregation, vividly affect the size, morphology, and properties of the products, (iv) The super-saturation conditions essential to persuade precipitation are usually the result of a chemical reaction. As such, any reaction conditions influencing the mixing process, such as rate of reactant addition and stirring rate, must be considered relevant to product size, morphology, and particle size distribution [66-72]. Chemical precipitation are comprise of 3 steps: chemical reaction, nucleation and crystal growth. It is not a controlled process. Lot of nanomaterial have been synthesized using this method mostly metal, metal oxide, Ferrite etc. can be synthesized. Nickel oxide nanoparticle has been synthesized by this method (73) ZnO has been synthesized by direct precipitation method using Zinc nitrate and NaOH as a precursors. (74). Ferrite nanoparticle has been formed by chemical precipitation method (75) Nb<sub>2</sub>O<sub>5</sub> has been synthesized by this method (76)

Thus chemical precipitation method can be used to synthesize many nanomaterials for nanomedicine, which can curb menace of risk of Covid 19

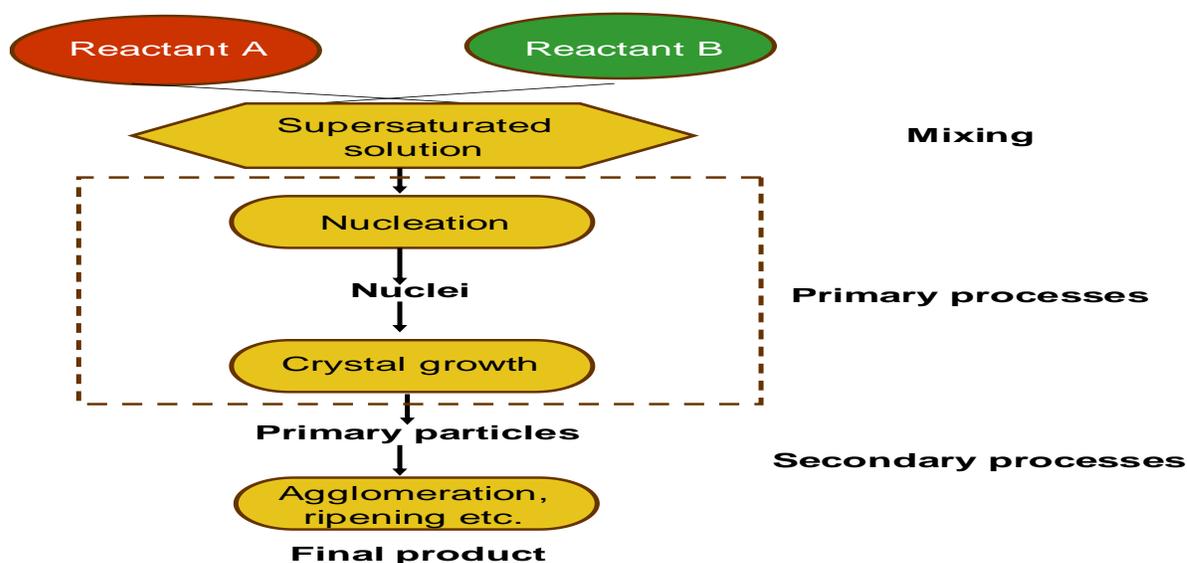
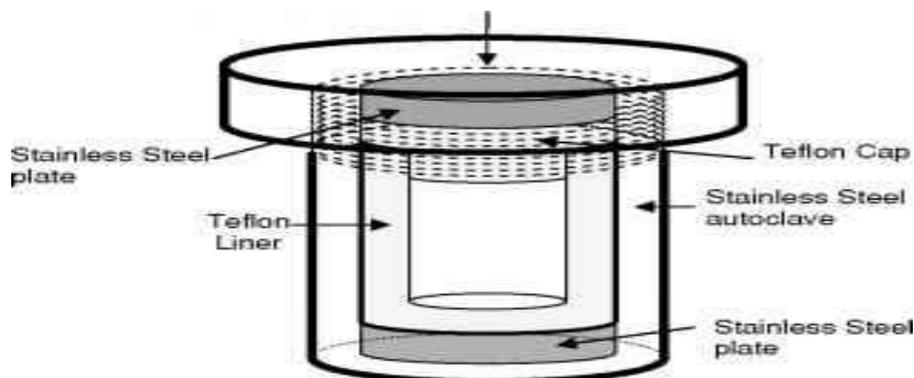


Figure 7: Scheme of precipitation process.

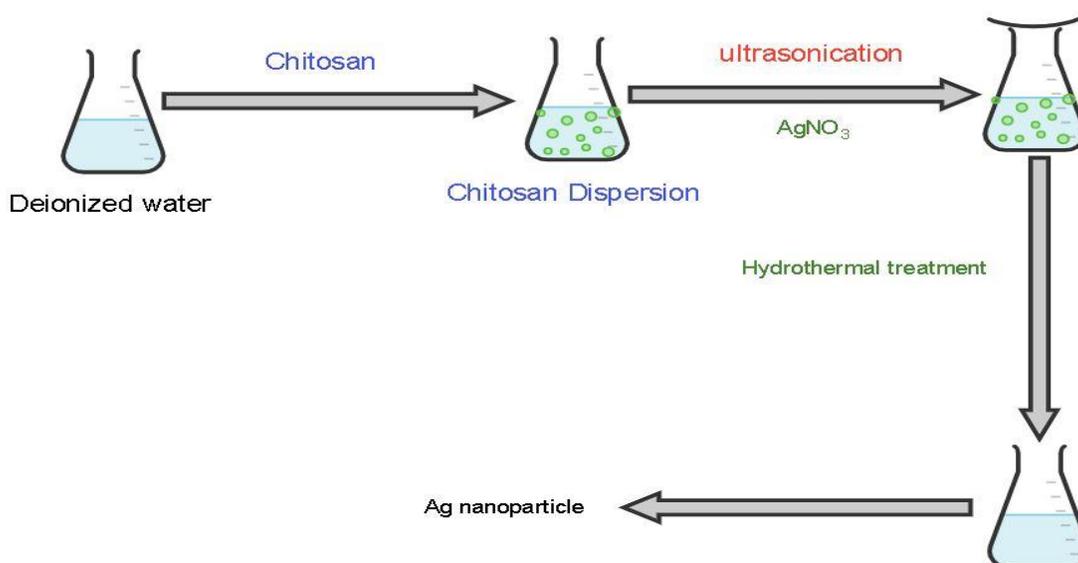
### Hydrothermal Method

Hydrothermal synthesis is a method of synthesis of single crystal material that depends on the solubility of crystals in hot water under high pressure. The crystal growth is executed in an apparatus entailing of a steel pressure vessel called an autoclave (**figure 8**), in which a precursor is supplied along with water. Many nanomaterials have been obtained such as metal oxide, ferrite, carbon quantum dots, VO<sub>2</sub> etc by hydrothermal method (77). Liquid phase or multiphase

chemical reaction can be able to control the composition of nanomaterial, synthesized by hydrothermal method. The morphology of the nanomaterial can be controlled by vapor pressure of the main composition of the reaction (77)



**Figure 8** Stainless autoclave for Hydrothermal



**Figure 9:** Scheme for Hydrothermal Method for synthesis of Ag nanoparticle

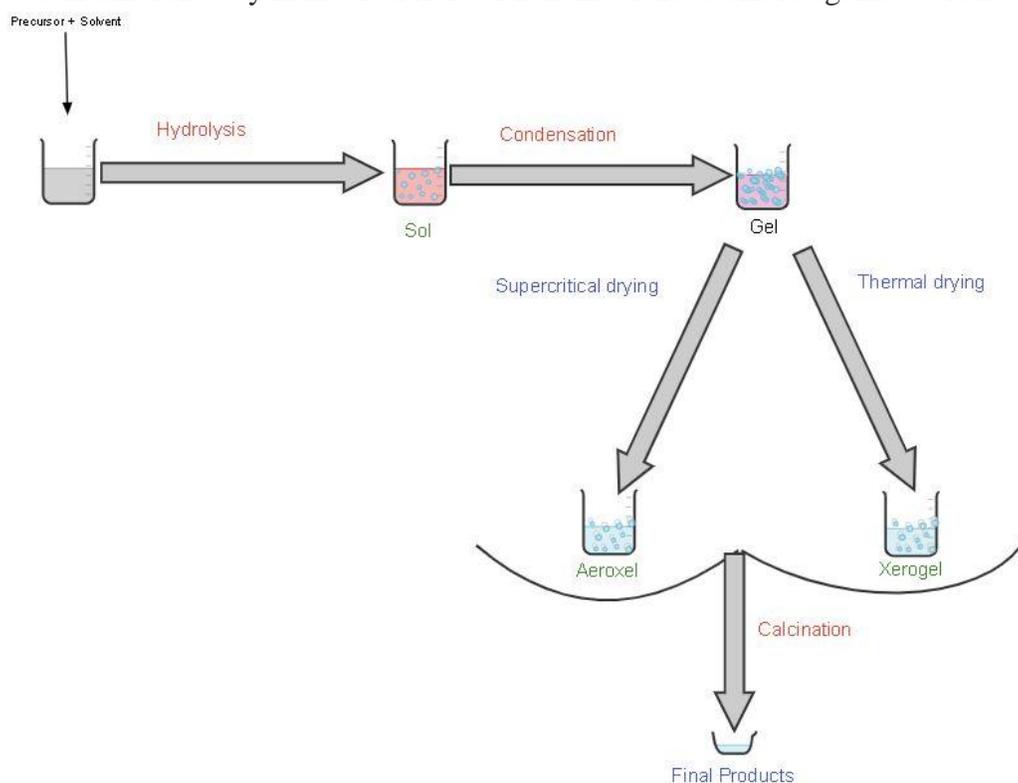
Thus nanomaterial with desired morphology, composition and shape applicable for coating, spraying, diagnostic kit, Drug, Drug delivery and therapeutics for curbing SARS-CoV-2, can be synthesized using Hydrothermal method

### Sol-Gel Method

As the name suggests, two types of materials involve in sol-gel. M. Ebelman synthesized in 1845. But it is last one or two decades considerable amount of interest has generated due to several advantages of sol-gel. First sol-gel process is generally a low temperature process means it requires less energy consumption. Some of the other benefits like obtaining unique materials such

as aerogels, xerogels, zeolites, ordered porous solid by organic-inorganic hybridization are exclusive to sol-gel process. It is also possible to synthesize nanoparticles, nanorods, nanotubes etc. using sol-gel technique. Sols are solid in a liquid. Gels are continuous network of particles with pores filled with liquid. Sol-Gel in general involves hydrolysis, condensation and polycondensation to form particles. **(Figure 10)**. Many nanomaterials synthesized have been by sol-gel method

TiO<sub>2</sub>, SnO<sub>2</sub>, WO<sub>3</sub> and ZnO have synthesized by sol gel method (78). SiO<sub>2</sub> nanoparticle which has great affinity towards RNA of Corona Virus, has been synthesized by Sol-Gel method(79). Thus sol-gel method is useful synthetic route for synthesis of various nanomaterial which used or will be used in different way in medical field or nanomedicine as shield against Corona Virus.



**Figure 10: scheme for Sol-Gel method**

### Conclusion:

Covid 19 has created havoc among people across the world and it is not getting diminish. Day by day, more people are being infected. So early detection and essential treatment become indispensable. Nanotechnology and nanoparticle have great prospect for minimizing the menace of Covid 19. Strategic use of nanoparticle in biosensors, spraying, coating, Drug delivery and Therapeutics require to develop quality product to fight against Corona Virus. Nanoparticles possess that eminence. Composition and morphology are very important to make desired product so that it will be effective. Synthetic technique would give yearning morphology like fiber, rod, sheet etc. Synthetic route is also important to make product economical so that it



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