

## Research Article

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## Analysis on Possible Influences of Characteristic of Nanoparticles on Behaviors of COVID-19 in Infection and Caused Disease, and Possibility of Using NP-DDS for Prevent Infection of COVID-19 and Treat its Diseases

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**Abstract**

Based on the analysis of the chemical composition and morphology structure of the New Coronavirus Disease-19 (COVID-19), it should belong to the protein nanoparticle with spherical complex structure. Thus, the COVID-19 should possess the physical and chemical properties of super large specific surface and super strong permeability. On the basis of this understanding, the rapid transmission speed and strong infectivity caused by its physical and chemical characteristics, as well as the reasons why the COVID-19 has more toxic, faster transmission speed and more infectious phenomenon than that of Sars virus are discussed. In addition, the ways that the COVID-19 infects people except via the route of the mouth, nose and respiratory tract system, but also can via the possible route that to enter the body through sweat pores to infect people, are also discussed. On the other hand, that the possible effects of the super strong permeability characteristics of the COVID-19 on the incubation period, asymptomatic infection, and different complications, syndromes, sequelae and other phenomena are also discussed in this paper. Finally, suggestions to further improve the prevention of the COVID-19 infection and improve the treatment effect of the COVID-19 diseases are put forward.

**Keywords:** New Coronavirus Disease-19 (COVID-19); Severe Acute Respiratory Syndrome Coronavirus 2; Nanoparticles; Penetrability; Infection; Prevention; Treatment

## Introduction

At the first, the author wants to note that this article is neither a research report nor a review. That is only author personal understanding and view as well as author self-sense perception which based on the observed and reported phenomena in the COVID-19 Epidemic. So that some of them are lack of evidences and needed to be proven yet. The purpose of this article is only hope to explain that many questions of the COVID-19 Epidemic maybe related with other academic fields except medicine branch of learning. So, during resolve problems shown in the COVID-19 Epidemic to combine point of other views such as physiochemistry science, biomedical materials and engineering science, is also suggested.

As well known that since COVID-19 has been discovered in 2019, it has spread to more than 230 countries and regions. By the early of September 2022, confirmed COVID-19 infects are more than 603 million and more than 6.48 million deaths [1]. So, the COVID-19 has become the largest global disaster in recent decades. Now, the researches on the detection methods, preventive vaccines and therapeutic drugs of the COVID-19 have been vigorously carried out accordingly, and many effective results have been obtained, which have played a great role in preventing the COVID-19 infection, treating Severe acute respiratory the syndrome coronavirus 2 (SARS-CoV-2) and reducing the case fatality rate.

Now, according to the medical community consensus, the COVID-19 is a virus, which is enter the body through the mouth, nose and respiratory systems and causes infection and then lead to causes disease of the SARS-CoV-2. Therefore, now mainly both methods of pathogen detection and nucleic acid detection are proposed to determine whether peoples are infected by the COVID-19 or not. According to the testing result to distinct the person that had not COVID-19 found as "Negative", and that the person had COVID-19 found as "Positive". On the other hand,

for the person who also is "positive" result but without any clinical symptoms of COVID-19 infection is called "Asymptomatic infection". And for the person who with both of "Positive" results and clinical symptoms is called "Confirmed cases". However, since for some COVID-19 infectors the clinical symptoms have appeared after several days of the COVID-19 detection, that is a period will exist between the COVID-19 detection and clinical symptoms appear. This period is called "Viral incubation period". Usuary, the "Incubation period" that between the infection by the COVID-19 to clinical symptoms discovered is about 1~2 until 10~12 days. Because during the incubation period the COVID-19 is also somewhat infectious, so that to early detect the COVID-19 infection and prevent further spread of the virus are still important. Therefore, formulated accordingly a 14-day medical observation period is stipulated, and the corresponding measures that require multiple rounds of nucleic acid testing [2-5].

Based on the mentioned above, it can be found most of the explanations and understanding are basically based on Virology and Infectious disease, and rarely discussions on the reasons that why these phenomena caused. Therefore, in this paper the author try based on point of physical chemistry and materials science views for analysis and discussion the possible influence of the physical and chemical characteristics of the COVID-19 on cause the COVID-19 epidemic the phenomena of the infection and the mechanism of pathogenesis.

### **The chemical composition and morphological structure, as well as possibly possessed physical and chemical characteristics of COVID-19.**

According to the medical community, COVID-19 is a virus composed of S protein trimer with obvious peripheral peaks such as coronavirus. Therefore, COVID-19 is called Coronavirus. However, according to chemical composition of the COVID-19, it is a kind protein substance.

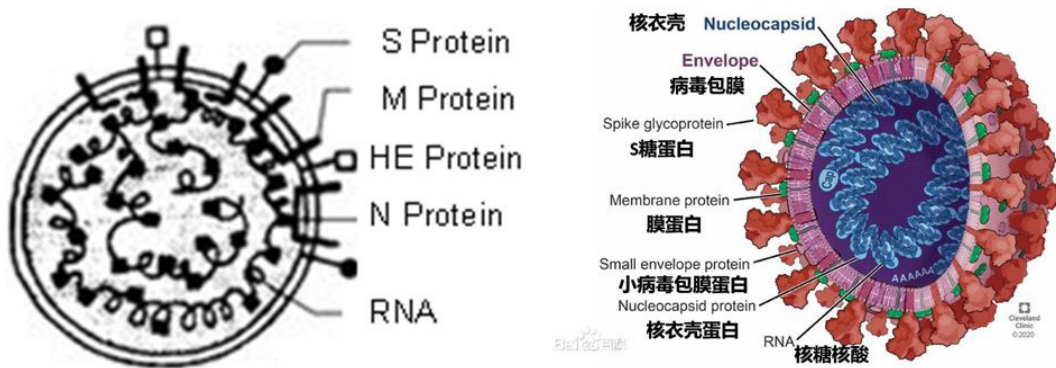


Figure 1: Composition of the COVID-19 [6-7]

Furtherly, considering the size of the COVID-19 is 80~120nm [8,9], that is within "solid particles between 1 and 100nm belong to nanoparticles" [10] definition range. So that, the COVID-19 is also a kind protein nanoparticle. Since proteins are made of amino acids, and the molecular structure of amino acids, the nanoparticles is both hydrophilic and hydrophobic substance. That lead to the COVID-19 can have certain affinity between the COVID-19 and the different hydrophilic and hydrophobic surfaces, such as surfaces of skin, various clothes and utensils, and then attach onto it.

It is reported, that nanoparticles (NPs) have many kinds of classifications. According to the material of the NPs can be classified as natural, synthetic, metal, non-metallic, organic,

inorganic, biodegradable and nonbiodegradable NPs. From its morphology can be classified as spherical, ellipsoidal, stick and fibrous NPs. And from its structure can be classified as solid, hollow, smooth surface, porous and complex structure NPs [11]. So that, based on the morphological structure of the COVID-19 shown in Figure 1 [12, 13], the COVID-19 should belong a kind spherical complex structured protein nanoparticle virus.

On another hand, considering all of nanoparticles have common characteristics of the super large specific surface and super strong permeability [14, 15], therefore, the COVID-19 should also possess the common characteristics that the super large specific surface and super strong permeability of the nanoparticles.



Figure 2: The COVID-19 [12, 13]

**Possible influences of physical and chemical characteristics of the COVID-19 on character of the virus transmission**

Based on the view of the COVID-19 is a kind protein nanoparticle substance, and the view of material science that the characteristics of any substance are closely related to the material and morphology of the substance. It can be considered that some behavioral characteristics of the COVID-19 observed in the epidemic should also relate with physical and chemical characteristics of the COVID-19.

In this epidemic, the phenomenon that the COVID-19 possess stronger toxicity, faster transmission, wider range of infection, as well as it even exceeds the Sars virus is found. The author considers that although effect of transmissibility depends on several factors such as susceptibility of individuals, viability of the virus in air, and interaction between the virus and the host so that, for example, different SARS-CoV-2 variants can have different transmissibility even if they have essentially the same size. So that the reasons for cause the phenomenon not only due to different toxicity existed between the COVID-19 and the

Sars virus themselves, it maybe also depended on the different morphology structure between both of the viruses.

According to the natural phenomenon, that the smaller dust is easier to be bellowed away, and faster to be bellowed to the farer place. So that it is considered that because average size of the COVID-19 is 60~140nm, but size of the Sars virus is 60~220nm [16], which is smaller and lighter than the Sars virus. So that result in the air, the COVID-19 and its aerosol will be faster blow and float to much wider range than that of the Sars virus, that is similar as the phenomenon observed in the epidemic.

On the other hand, although both of the COVID-19 and Sars virus are nanoparticle, but since smaller size nanoparticle has stronger penetrability, as shown in Table 1. So that the penetrability of the COVID-19 is stronger than that of Sars virus. Result in to leads the damage of the COVID-19 to organs and tissues of the patient is also higher than that of Sars virus. Finally, it became the observed phenomenon such as the COVID-19 is a virus with more virulent, faster transmitted and more contagious, that compared with that of Sars-19 virus.

Table 1: Different sizes particles can reach location in vivo [17]

Particle size	Can reach the location <i>in vivo</i>
>12 mm	Can be blocked at the end of the capillary or stay in the liver, stomach, as well as in the organs with tumors
7~12 mm	Can be ingested by the lungs by intravenous injection
2~12 mm	Can be ingested by capillary network, not only can reach lung, but also can reach liver and spleen
1 mm	The size is most likely to be devoured by white blood cells
0.1~0.2 mm	Can be injected through the vein, artery or abdominal cavity, and in the reticuloendothelial system be absorbed by macrophages from the blood
< 50 nm	Can be transmitted through the liver endothelium or through lymph to the spleen, and can also reach bone marrow, as well as tumor tissue and liver

**Possible influences of physical and chemical characteristics of the COVID-19 on infection route of the COVID-19**

Now the current consensus on the route of the COVID-19 infection have three transmission modes. They are direct transmission, aerosol transmission, and contact transmission. However, author consider that maybe one more COVID-19 infection mode, which related with physicochemical properties of the COVID-19 itself should be also need to be considered [18].

As mentioned above, that the size of the COVID-19 is 60~140nm, but the size of human skin sweat pore aperture is 20,000~50,000nm [19]. That means size of the COVID-19 that only one percent of human skin sweat pore aperture. Considering the density of sweat pores on the human skin is as high to 100~120/cm<sup>2</sup>. Only the number of sweat pores on human's face alone is more than 20,000, so that the number of the whole body is countless.

On another hand, because the sweat pore is a kind small channel or long hair holes which is sebaceous glands secreted oil flow into on skin surface. So, there is a good affinity existed among the lipophilic skin and the sweat pore wall with the both hydrophilic and hydrophobic COVID-19. And the size of the sweat pore is hundred times big than the COVID-19, which lead to the COVID-19 can easily pass through the sweat pore. Therefore, the author considers that, due to both hydrophilic/hydrophobic properties and strong penetration of COVID-19, another COVID-19 infection route possibly exists, that is first the COVID-19 attaching to the skin surface, entering the sweat pore, and then penetrating into the body through the sweat pore.

### **Possible influences of physical and chemical properties of the COVID-19 on caused disease**

It is well known that the symptom of the COVID-19 infections mostly is cough and fever. It can be considered that because most of the patients are infected the COVID-19 by the route of mouth, nose, respiratory system into the body, so most of the COVID-19 can directly reach into the lungs. It results in the lungs have the most amount of the COVID-19, and firstly reach the virus amount to cause the disease in the lungs. Thus to form the phenomena that earliest inflammation is in the lung, and then to cause into the SARS-CoV-2.

Considering the COVID-19 is also a kind nanoparticle, its super strong permeability should be able also to be penetrated into organs and tissues of the COVID-19 infector, and without goal moved from one organ and tissue to another organ and tissue in the body. Resulting in damage to various organs and tissues of the COVID-19 infector.

Because there are many factors can influence the COVID-19 detection result, which as detection method, detection object, sampling object, sampling position, sensitivity and accuracy, as well as the personal differences among each the COVID-19 infectors, etc. It leads to form different time interval between infected by the COVID-19 and detected the person has been infected by the COVID-19, which finally to exist an "Eclipse period" from 1~2 until 10~12 days between the infection by the COVID-19 to clinical symptoms discovered. So that, some of the COVID-19 infected persons need multiple nucleic acid tests to confirm themselves infected or not. However, it is also found that the test results of some the COVID-19 infected persons

suddenly change from "negative" to "positive", even to appear the phenomenon that some of the COVID-19 infected person after recovery will suddenly change from "negative" to "positive" again. So that, to call the COVID-19 infected person who had not clinical symptoms discovered as "asymptomatic infections", and to the person had discovered clinical symptoms as "definite cases". For the phenomenon that some the COVID-19 infector suddenly changed from "positive" to "negative", it is considered that maybe is due to the COVID-19 in their body had been killed by antibodies of the infector himself before the varus reaches enough amount to cause the disease.

On the other hand, due to average diameter of the human normal cells is 5~200 million nm [20], that is hundreds to thousands of times larger than size of the COVID-19. Therefore, it can be thought over that the COVID-19 not only possibly penetrate into various organs and tissues of the infector, but also possibly continually drill into cells of the organs and tissues, as well as moved from one cell to another cell, which to cause damage to the normal cell adhesion, growth and reproduction behavior, and lead to the cell variation and apoptosis, until the tissues and organs lesions. Therefore, it may be one of the factors, that to cause other complications and syndromes [21], as well as the reason that after the person recovery to cause the Sequel in smell, nervous system, skin and other tissues and organs [22].

It is reported that the presence of COVID-19 was found in the brain of a person who had died for 200 days of SARSCoV2. According to the understanding that the COVID-19 possess super penetrability can penetrate into the human organs and tissues, it can be considered that due to the COVID-19 can constantly replicate in the human physiological environment and maintain a certain viral activity. Therefore, these COVID-19 maybe have drilled into the brain before his death or slowly after his death. So that, it is estimated that if a long-term, multi-organ and tissue sampling analysis of the deceased infected with COVID-19 or its variants, the presence of COVID-19 or its variants may also be found in the other organs and tissues of the deceased.

Further, after discovered the COVID-19, many mutants the COVID-19, such as Alpha, Delta, Omicron etc. it have also been discovered, and some of them have stronger toxicity and greater infectivity than that of the COVID-19. It has also found that the Omicron can keep survival time on the plastic surface for survive 8 days, that much more than the COVID-19 only for 56 hours survival time (Figure 3) [23].

(Unit: Hours; Condition: 25°C; Humidity 45~55%)

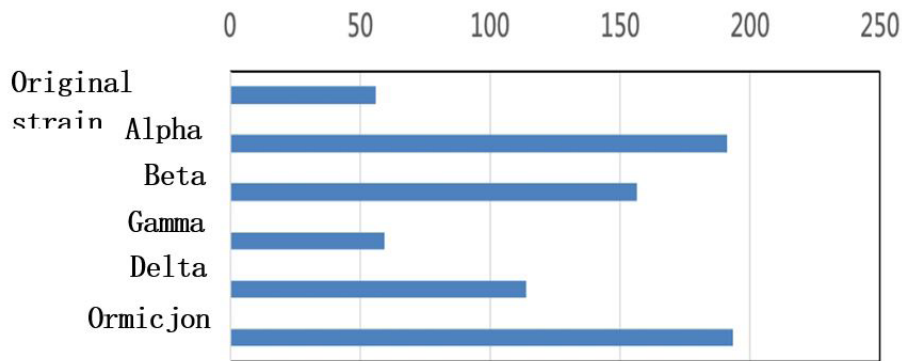


Figure 3: Survival time of COVID variant strains on plastic surface [23]

Whether the causes of these phenomena are also related to the differences in the chemical composition and morphology structure of these mutant strains with the COVID-19, it needs to be further observed and accumulated with more information.

### Suggestions on improving the prevention of the COVID-19 infection and improving the efficacy of diseases caused by the COVID-19

Now, in order to prevent infection of the COVID-19, except to taking vaccines to improve their immunity, they basically advocate wearing masks and goggles outside, keep a certain distance between people and people, wash hands immediately and frequently after entering the in to the room, etc. are well advocated [24, 25]. However, considering the hydrophilic hydrophobicity of COVID-19 can lead to attach onto surfaces of the skin and clothing and existence of another infection route of the COVID-19 into the body, i.e., via sweat pores of the person into the body. As well as, because human head (including head, face, neck, eyes ears) and hands are the parts of the body exposed outside with the biggest surface for the longest time. So that, except the precautions mentioned above, it is also recommended that to separately place the indoor and outdoor clothes, to wear hats, scarves, gloves and long clothes as much as possible outside as possible as can to minimize the skin to exposure outside, as well as to wash the exposed face, neck, eyes ears.

In addition, in order to enhance the barrier efficiency of the mask on the COVID-19 and its mutant strains, the material, shape and coverage area of the mask, as well as the quality standard of the mask, should to be further improved. Meanwhile, the detection method, sampling, and the sensitivity and accuracy of the COVID-19 were further standardized and unified.

On the other hand, given that the Nano-particle Delivery System (NP-DDS) can not only facilitate the continuous release and targeted release of drugs, to reduce the applied number of drugs and eliminate the possible side effects of general dosage forms. Moreover, because the super-large specific surface of the NP-DDS can increase the contact area of the drug with the lesion site, improve the drug concentration into the lesion site and continuously release the drug, it has the advantages of improving the drug utilization rate and the drug effect of [26, 27]. Nowadays, the NP-DDS has been widely used in clinical medicine, such as cancer treatment of [28, 29], gene therapy of [30], and intracellular targeted administration. etc. [31]. Since the technical in the condition of without additives [32, 33] prepared NP-DDS can not only maintain a good dispersion and stability in water, but also can keep the purity of the released drug [34, 35].

Considering affinity of the lipophilic the NP-DDS carrier with the organism, as well as the super penetration of the NP-DDS, result in the NP-DDS can conglutin and penetrate into the mouth, nasal cavity and ocular mucosa. It will helpful to realize that the continuous releasing drug and keeping a certain concentration of the drug in the mouth, nasal cavity and ocular mucosa. In this way can more effectively block the COVID-19 infect route that from the mouth, nose, respiratory system and through the eye mucosa into the body, to improve the prevention effect of drugs on novel coronavirus infection. Therefore, it is recommended that to research and develop NP-DDS pharmaceutical preparations of prevent and the treating COVID-19 and its mutant virus caused diseases. Then further to produce their NP-DDS injection-preparation, spray-preparations, drop-preparations and ointment-preparations, and by using injecting the NP-DDS injection-preparation into the body, spraying the NP-DDS spray-preparation into oral, dropping the drop-preparation into

oral, nasal and eyes, as well as daubing the ointment-preparation into nose and eyeball, for achieve the goal of prevent infection of COVID-19 and its mutant virus, and treat the disease caused by them. Because by using the NP-DDS preparations not only can keep the drug concentration in the lesions part for a period of time, but also can avoid the possible side effects of the conventional drug preparations to the normal tissues and organs. So, it can greatly improve the prevent and treatment effects of the drugs [36, 37].

To sum up: it can be found that many phenomena caused in the epidemic of the COVID-19 had related with the characteristics of the COVID-19 which depended on the chemical composition and morphology structure of the COVID-19. And some of the phenomena can also be explained by characteristics that it is a protein nanoparticle super small size, super large specific surface and super strong penetration of the COVID-19 possessed.

It explains that to prevent infection of the COVID-19 and to treat the diseases caused by the COVID-19 is not only a research subject of the medical science, but also a research subject for multidisciplinary researches such as physical, chemistry and material science, etc. So, it is necessary to fully understand the characteristics of the COVID-19. And to cooperate multidisciplinary experts for further developing the detection methods and prevention technologies of the COVID-19. By the way of early finding the COVID-19 infected persons and taking the corresponding measures to stop the further spread and spread of COVID-19, as well as to apply more efficient pharmaceutical preparations for improving the treatment effect of preventing infection of the COVID-19 and of the treatment effect of treating diseases caused by the COVID-19. It will be useful for soon eliminate the global disasters caused by the COVID-19 and its variant strains.

On the other hand, it should be noted that because the coronavirus Epidemic development of sudden and urgent, lead to some preventing COVID-19 vaccines and treating SARS-CoV-2 drugs have been emergency approval given application in clinical, but due to some of them are still during clinical trial time and haven't sufficient data to demonstrate their effectiveness, safety and understand their side effects, especially after medication may produce sequela is not completely clear. Therefore, due to avoid sequelae of these vaccines and drugs become second serious disease after the COVID-19 epidemic outbreak, it is necessary to

further research and understand the possible sequelae produced by these vaccines and drugs, as well as the corresponding countermeasures.

Finally, it is also suggest that given that almost all viruses are of very small sizes, larger viruses are 300~450 nm in diameter, and smaller viruses are only 18~22 nm in diameter [38]. And the smaller virus is also within the range of nanoparticles, that they also a kind protein nanoparticle. Therefore, the question of whether the characteristics of the nanoparticles of these viruses will have some impact on their infectious behavior, possible diseases, complications and sequelae, is also a topic that should be further considered and recognized.

## Conclusion

According to the protein composition and morphological structure of the COVID-19, it is a kind protein nanoparticle virus with a spherical and complex structure, and possesses the characteristics of the super large specific surface and the super strong penetrability. The ultra-small particle size of the COVID-19 may not only be an important factor in its fast spread speed, large spread range and strong infection, but also may be another infection route that enables it to invade the human body through sweat pores. The strong penetration of the COVID-19 may allow it to enter different organs and tissues in the infected person and even drill into the cells to cause normal cells variation and apoptosis, resulting in damage to different organs and tissues; it may be a factor to cause other clinical complications, syndrome and sequelae in addition of the SARS-CoV-2.

On the other hand, due to the COVID-19 can pass-through different route and need different time to reach the nucleic acid detection site and the lesion site in the body, and because for different the COVID-19 infector the time to reach the necessary amount of the pathogenic virus for achieving the nucleic acid detection and to cause the pathopoeia maybe also different. Additional, since the individual differences between each the COVID-19 infected person. Maybe it is one of the factors for causing phenomena of the different "incubation period", "asymptomatic infection", "confirmed cases" and different complications, syndrome and sequelae.

So that, due to prevent the COVID-19 infection, it is recommended that to minimize exposure skin to outside, to fabricate and apply inject-, spray-, drop- and ointment-nanoparticle preparations.

In addition, it is suggested to further standardize the detection method, sampling site, sampling method and judgment criteria of the COVID-19, as well as to further improve the sensitivity of the detection reagent, the accuracy of the test method, and shorten the time of the detection process.

Finally, in order to fully understand the causes of COVID-19' wide transmission range, rapid transmission speed, strong viral infectivity and may to lead to variety of diseases, it is necessary conducting multidisciplinary collaborative research. Only by this way, that the treatment measures to prevent COVID-19 transmission and various diseases caused by COVID-19 can be successful.



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