



ORIGINAL ARTICLE

Possible Effect of Nano Characterization of COVID-19 on Infection and Causing Disease

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Abstract

In this article, based on analysis of chemical composition and morphology structure of the New Coronavirus Disease-19 (COVID-19), that the COVID-19 belongs a kind protein nanoparticle virus with spherical complex structure has been explained. So, the COVID-19 possesses characteristics of ultra-small size, large specific surface, both hydrophilicity and lipophilicity, that just as all of the nanoparticles. It leads to the COVID-19 producing fast spread speed, large spread range and strong infection, as well as possibly to lead to another infection route that enables it to invade the human body through sweat pores. Based on this understanding, the rapid transmission speed and strong infectivity caused by its physic-chemical characteristics, the reason of the COVID-19 has more toxic, faster transmission speed and more infectious phenomenon than that of SARS virus are discussed. On the other hand, that the possible effects of characteristics of the COVID-19 on the incubation period, asymptomatic infection, and different complications, syndromes, sequelae and other phenomena are also discussed. Finally, the proposes for further improving prevention of the COVID-19 infection and 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, Nano-Particle Delivery System (NP-DDS)

Introduction

It is reported 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 that the COVID-19 has become the largest global disaster in recent decades.

Now, the common recognition to COVID-19 is a virus

and is enter the body through the respiratory systems and causes infection and finally lead to causes disease of the SARS-CoV-2. Therefore, now mainly both methods of nucleic acid detection and pathogen 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].

According to the mentioned above, it can be found that although the route for COVID-19 infection and the phenomena when after a person had been infected by the COVID-19 had been mentioned, but the reasons for leading to these phenomena are still not clear and have not been explained yet. So that, the author



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tries to discuss them based on the views of materials, biomedical science and engineering disciplines, in this article.

About Belonging and Characteristics of COVID-19

According to the medical classification, COVID-19 is a virus and is called Coronavirus which because composition and structure of the COVID-19 has composed of S protein trimer with obvious peripheral peaks. However, according to chemical classification of the COVID-19 that based on its composition, the COVID-19 belongs a kind protein substance.

Furtherly, considering size of the COVID-19 is 80~120 nm [6,7], that is within “solid particles between 1 and 100 nm belong to nanoparticles (NPs)” [8] definition range. So that, the COVID-19 is a kind NPs, and it is a kind protein NPs. And based on morphology structure of the COVID-19 as shown in Figure 1 [9], the COVID-19 belongs a spherical complex structured protein NPs virus.

Considering all of NPs have common characteristics that the super large specific surface and super strong permeability [10,11], therefore the COVID-19 should possess the common characteristics that the super large specific surface and super strong permeability of the NPs. It means the possibility is exist, that for the protein type NPs the COVID-19 to penetration and entry into the body, and further into various organs and tissues of the body.

On the other hand, because all protein molecule contains amino acid component, it will lead to the protein becomes a kind **biparental** substance. Therefore, as a protein type NPs, COVID-19 is also a kind biparental substance, and COVID-19 possesses both hydrophilicity and **lipophilicity**. It means the COVID-19 possesses

affinity with various surface such as surfaces of skin, clothes and utensils, and even can to attach onto them.

About Effect of COVID-19 Characteristics on its Disseminate and Infection

Now the current consensus on disseminates and infection of the COVID-19 is by the route of direct transmission, aerosol transmission, and contact transmission. However, since size of the COVID-19 is 60~140 nm, but the size of human skin sweat pore aperture is 20,000~50,000 nm [12]. Since the pore size of the human skin sweat pores is more than several hundred larger than that of COVID-19, it means the COVID-19 can easily go to inside of the human skin sweat pores. Furtherly, due to density of sweat pores on the human skin is as high to 100~120/cm², 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. In the case, so many attached on skin COVID-19 can enter into the body from the sweat pores, and then the COVID-19 can enter into the body by pass through the small and long channel hair holes of the sweat pore.

Therefore, it can be considered that except the current consensus on disseminates and infection of the COVID-19 is by the route of direct transmission, aerosol transmission, and contact transmission, maybe existed an another COVID-19 infection route. That is the COVID-19 firstly attach onto the skin surface by its both hydrophilic/lipophilic properties, and then enter into the body through sweat pore and by its strong penetration [13].

About Effect of COVID-19 Characteristics on Character of the Virus Transmission

Based on the view of characteristics of any substance are closely related to the material quality and morphology of the substance, behavioral characteristics

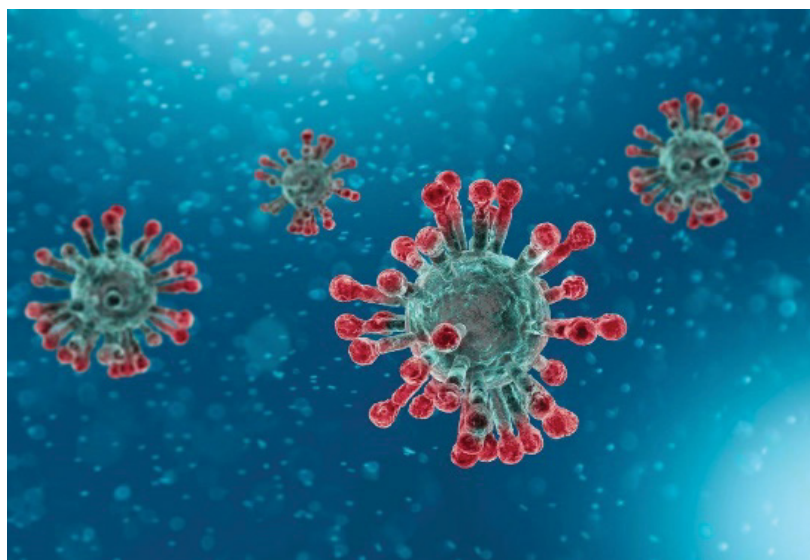


Figure 1: The COVID-19 [9].

of the COVID-19 observed in the epidemic should also relate with physical and chemical characteristics of the COVID-19.

In this epidemic, it is observed that the COVID-19 possess strong toxicity, fast transmission and wide range of infection, which even exceeds the SARS virus. Author thinks that the cause to produce the phenomenon except depended on the different toxicity between the COVID-19 and the SARS virus themselves, maybe also depended on their different morphology structure. That is since average size of the COVID-19 is 60~140 nm, but size of the SARS virus is 60~220 nm [14], which is smaller and lighter than the SARS virus. So that result in the air, COVID-19 and its aerosol can be faster blow and float to much wider range than that of SARS virus. It just likes the natural phenomenon that smaller dust is easier to be bellowed away, and faster to be bellowed to the farer place.

On the other hand, as shown in Table 1 [15] that smaller size NPs have stronger penetrability and can penetrate to deeper organ and tissue in the body. Therefore, although both COVID-19 and SARS virus are NPs, but since COVID-19 is smaller than that of SARS virus, the penetrability of the COVID-19 is stronger than that of SARS virus. It leads to the damage of the COVID-19 to organs and tissues of the person are also higher than that of SARS virus. Finally, to produce the observed phenomenon that the COVID-19 is a virus with more virulent, faster transmitted and more contagious, that compared with that of SARS-19 virus.

About Effect of COVID-19 Characteristics on Caused Disease

It is reported that the symptom of the COVID-19 infections mostly is cough and fever. Author considers that because most of the patients are infected the COVID-19 by the route of mouth, nose, respiratory system, so most of the COVID-19 has directly reached into the lung. It let most amounts of the COVID-19 gathers in the lung to reach the virus amount for causing disease. Result in produce the phenomena that the lung is earliest causing the inflammation and then developing to the SARS-CoV-2.

Considering the COVID-19 is a kind NPs, so super

strong permeability of the COVID-19 should also can penetrate into person's organs and tissues, then without goal move from one organ and tissue to another organ and tissue in the person's body. Result in damage to various organs and tissues of the COVID-19 infector. However, because detection result of the COVID-19 can be affected by many factors, such as detection method, detection object, sampling object, sampling position, sensitivity and accuracy, as well as the personal differences among the COVID-19 infectors, etc. In result produced the "Incubation period", i.e., a time interval from a person had been infected by COVID-19 to decide this person had infected by the COVID-19. For example, since a person can infect COVID-19 via different infection route, so the COVID-19 can via different way to entrance inside of person and reach different position of the body. That result in the COVOD-19 needs different time to reach the sampling position and disease site, as well as also need different time to reach the enough COVOD-19 amounts for determination and cause disease. Finally, to produce about 1~2 to 10~12 days' Incubation period, that just like the observed phenomenon.

On the other hand, considering average diameter of the human normal cells is 5~200 million nm [16], that is hundreds to thousands of times larger than size of the COVID-19. It means in a person's body the COVID-19 not only can penetrate into various organs and tissues, but also can drill into cells of the organs and tissues. The COVID-19 can move in the body from one organs and tissues to another organs and tissues, and from one cell to another cell, which to cause damage more organs, tissues and normal cells. Since adhesion, growth and reproduction behavior of the cells had been damaged, result leads to the cell variation and apoptosis, until the tissues and organs lesions, that even to cause cancer of the tissues and organs. So, it is considered that maybe it is one more factor for causing other complications and syndromes [17], as well as one of the factors for a person after recovery to cause the Sequel in smell, nervous system, skin and other tissues and organs [18]. It is considered that the reported phenomenon, that in a died by SARS-CoV-2 for more than 200 days person's brain found exist of COVID-19, is good support to the analysis above. Based on the above understanding, that the super penetrability of COVID-19 can penetrate

Table 1: Different sizes particles can reach location *in vivo* [15].

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

into human's organs and tissues, and can constantly replicate in the human's physiological environment to maintain a certain viral activity. So that the COVID-19 can continually move and drill into person's organ and tissue, which even in died person's body until the COVID-19 lost viral activity itself. Therefore, it is inferred that if we can perform a long-term, multi-organ and tissue sampling analysis of the deceased infected with COVID-19 or its variants, maybe can also find COVID-19 or its variants presence in died person's other organ and tissue.

Now many mutants of the COVID-19, such as Alpha, Delta, Omicron etc., it have been discovered. The phenomena that some of mutants have stronger toxicity and greater infectivity than that of the COVID-19, and 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 2) [19], have been also found. 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 for Improving Prevention of the COVID-19 Infection and Improving Efficacy of Diseases Caused by the COVID-19

Considering COVID-19 is a spherical complex structured protein NPs, that possess superpenetrability and is also a kind biparental substance possesses both hydrophilicity and lipophilicity. Therefore, in order to prevent infection of the COVID-19, except to put using the advocated methods, such as taking vaccines for improving immunity, wearing masks and goggles outside, keeping a certain distance between people and people, washing hands immediately and frequently after entering into room, etc. [20,21], it is also suggested that to avoid contact other person's skin and other matters for avoiding contact the COVID-19 maybe attached on them. Because the human head (including the head, face, neck, eyes, ears) and the skin of both hands are the longest time and the biggest human surfaces to

expose in the air. Therefore, to reduce exposed skin, it is recommended to wear hats, scarves, gloves and long clothes outside as much as possible. And as fast as possible also to wash the exposed hands, face, neck and eyes after entering into room. On the other hand, considering the hydrophilic hydrophobicity of COVID-19 can lead to attach on clothes and other objects, to separately place the clothes and other objects used indoor and outdoor is also recommended.

In addition, for enhancing barrier efficiency of mask to 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, due to Nano-particle Delivery System (NP-DDS) can not only facilitate the continuous release and targeted release of drugs, which can result in reduce the applied number of drugs and eliminate the possible side effects of general dosage forms. The super-large specific surface of the NP-DDS can also increase the contact area of 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 [22,23]. Nowadays, the NP-DDS has been widely used in clinical medicine, such as cancer treatment of [24,25], gene therapy of [26], and intracellular targeted administration. etc., [26]. Because the NP-DDS fabricated under condition of without additives [27,28] can not only maintain a good dispersion and stability in water, but also can keep the purity of the released drug [29,30]. It is considered that, in the case of using lipophilic polymers as a drug carrier to manufacture NP-DDS. By using lipophilicity of the NP-DDS carrier and the superpermeability of NP-DDS itself to enable NP-DDS to attach and penetrate into the oral, nasal and eye mucosa. This not only helps to realize drugs continuous release to maintain a certain drugs concentration in the oral cavity, nose cavity and eye mucosa, but also can more effectively block the infection route of COVID-19 from the mouth, nose and respiratory system into the

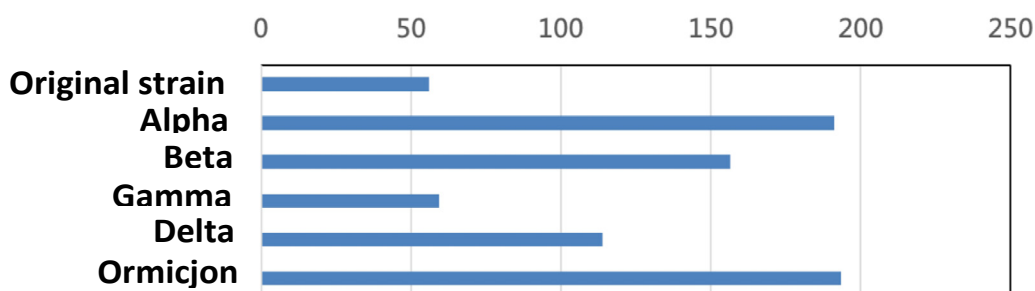


Figure 2: Survival time of COVID variant strains on plastic surface [19].
(Unit: Hours; Condition: 25 °C; Humidity 45~55%).

human body through the eye mucosa, so can further improve the prevention effect of drugs on novel coronavirus infection. Therefore, author recommends 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 [31,32].

To sum up: it can be seen that many phenomena caused in the COVID-19 epidemic is related with the characteristics of chemical composition and morphology structure, that the protein composing, nano size, both of hydrophilicity and lipophilicity, as well as super strong penetration of the COVID-19. And some observed phenomena can also be explained by the COVID-19's belonging that it is a spherical complex structured protein NPs virus. It explained that COVID-19 caused phenomena and disease is closed related with nano behavior of the COVID-19.

Conclusion

Based on composition and morphological structure of the COVID-19, the belonging of the COVID-19 is a kind protein nanoparticle virus with a spherical and complex structure can be recognized. So, the COVID-19 should possess characteristics of ultra-small size, large specific surface, both hydrophilicity and lipophilicity, as well as super strong penetrability. That result in the COVID-19 possesses fast spread speed, large spread range and strong infection, as well as can lead to produce another infection route that enables it to invade the human body through sweat pores. Because the strong penetration can allow the COVID-19 drill into inside of different organs and tissues, and even can furtherly drill into cells to cause normal cells variation and apoptosis, resulting in damage to different organs and tissues. It may be a factor to cause different 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. Therefore, it is proposed that during research the COVID-19 and COVID-19 caused disease, at the same time should connect research of nano behavior of the COVID-19.

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