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COVID-19 clinical implications: the significance of nanomedicine

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Summary

COVID-19 pandemic has profoundly affected the lives of humans worldwide. We no longer experience the same quality of life and need to come up with effective solutions to combat the clinical implications. The vast knowledge about the pathways that regulate the virus entry and molecular signaling of the pathogenesis of coronavirus are the key factor for the development of *de novo* diagnostic/therapeutic strategies. Meanwhile, the emergence of nanotechnology, could offer enormous help in the battle against coronavirus. In this editorial, the role of molecular elements in the pathobiology of the disease and the significance of nanoscaled pharmaceuticals is highlighted.

Authors' Biosketch

Jaleh Barar received her Ph.D. from Cardiff University (U.K.) and is currently a Full Professor and the Chair of the Department of Pharmaceutics at the Faculty of Pharmacy, Tabriz University of Medical Sciences. Professor Barar's research is focused on various aspects of pharmaceutical cell biology with a particular emphasis on the development of novel drug delivery and targeting strategies to combat cancer.

Despite the experiences in terms of viral infections and its social consequences, we all supersized with the worldwide spread and impacts of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a strain of coronavirus family. The coronavirus disease 2019 (COVID-19) pandemic has indeed imposed a deep influence not only in human beings but also in our viewpoints on the management of such hectic situations in all aspects. We know that the entry point of the SARS-CoV-2 is through binding to the receptor angiotensin (ANG)-converting enzyme 2 (ACE2),[1,2] which is overexpressed in various tissues and organs, including lung, kidney, heart, and gastrointestinal tract.[3] Once interacted with the ACE2 of alveolar/other cells via their spike (S1) protein, the virus can enter the cells and distribute through vesicular trafficking – a process that depends on the priming of the S protein by the serine protease, transmembrane protease serine 2 (TMPRSS2) of the host cells.

Different strategies should be considered for molecular targeted therapy of COVID-19. One important approach would be the inhibition of ACE2, to interrupt the virus integration with the cells. ACE2 is widely expressed on the apical membrane of testis, heart, liver, kidney, and also the brain. It appears to have a regulatory role in the pathophysiology of different diseases (i.e. cardiovascular, diabetes, and respiratory distress syndrome). Therefore, cascades of molecular events can happen because of the reduced functional expression of ACE2, and hence, alveolar cells can be injured resulting in the provocation of inflammatory responses in the lung and alterations in circulating leukocyte subsets and cytokine secretion.[4, 5] Thus, the question should be addressed is that the safety of the inhibition of the entry point of the virus, ACE2. So, the major question would remain a challenging issue "Is it safe to block the ACE2 locally on the surface of alveolar cells?" However, it is worthwhile to develop and examine multifunctional microparticles and/or nanoparticles containing a cocktail of drugs to control not only the entry of the virus locally but also to manage the devastating cytokine storm.

It is envisioned that targeted drug delivery to the infected cells via nano-structured cargo would be a reliable diagnostic/therapeutic strategy. Hence focusing on the cellular trail of the SARS-CoV-2 virus especially the sites of virus assembly and the endocytosis pathway seem to be

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a scientific challenge to combat this disease. The size of nanotherapeutics is a determinate factor in the governing factor on the cargo's final cellular destination. Since the endocytosis is the main mechanism of internalization for the nanoparticles, it is noteworthy to fabricate such particulate drug delivery system with optimal size to be seen by cellular uptake machinery (i.e., clathrin- and caveolae-dependent vesicles).[6] However, if the systemic route is the method of administration, the extravasation of nanoparticle and escape from the surrounding epithelial layer may be a restraining factor. On the other hand, pulmonary administration via inhalation can be an effective means of drug delivery/targeting of the infected lung epithelial cells. Thus, in parallel with the cellular uptake mechanism, the design of suitable cargo for the localization of the nano-therapeutic agents into the lower respiratory tract is essential.

Lastly, the development of prophylactic strategies for such emerging pandemic infectious diseases is equally important to the therapeutic approaches. In this regard, various research groups have conducted different approaches to design effective vaccines, including bioinformatics tools.[7]

As a concluding remark, we need to educate ourselves in terms of pharmacotherapy/prevention of any type of contagion outbreaks that seems to happen anyway.

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Competing interests
None.

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