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NANOTECHNOLOGY BASED APPROACH TO COMBAT COVID-19: SCOPES AND PERSPECTIVES

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Abstract: The viral outbreaks caused by SARS-CoV-2 has already spread around the world. The main characteristics of the virus include rapid mutation, cross species transmission and adaptation to various epidemiological conditions. The present outbreak has tested the limit of healthcare systems and present genuine questions about management using traditional therapies and diagnostic tools. In this regard the use of nanotechnology offers new opportunities for the development of novel strategies in terms of prevention, diagnosis and treatment of COVID-19. In this paper, with a brief description of various types of nanoparticles, that develop the technology, the nanotechnology-based strategies for rapid, accurate and sensitive diagnosis, the improvement of contact tracing tools, the production of effective disinfectants, the delivery of antiviral agents into the body and the possibility of developing nano vaccines has been presented. The limitations of nanotechnology-based approaches to combat COVID-19 also have been discussed.

Keywords: Drug delivery, Nanoparticles, Nano sensors, Nanotechnology, Nanovaccines. SARS-CoV-2.

Introduction

The violent disaster and pandemic that not only vibrate but at the same time, unite the whole world for its prevention, is caused by a virus which was first detected in Wuhan, China and termed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on February 11, 2020 [1]. Although initially the disease was reported to be pneumonia of different kind, but after a detailed investigation from all parts of the scientific world, it was established that the particular disease was caused by a type of coronavirus [2]. The far-reaching infection as well as transmission of SARS-CoV-2 sparked high alert and forced the WHO to declare a pandemic in March 2020 [3-4]. SARS-Cov-2 is an enveloped virus with a positive- sense single-stranded RNA. The genome sequence of this virus shows that nearly two-thirds of the RNA is composed of sixteen non-structural proteins along with polyproteins, whereas the rest one-third consists of four structural proteins – envelope (E), membrane (M), nucleocapsid (N) and spike (S) – which are responsible for forming nucleocapsid, thereby enabling the attachment of the virus to host cells by binding to angiotensin-converting enzyme 2 (ACE2) [5-7]. As the respiratory tract has the highest expression of ACE2, it is the main target of SARS-CoV-2 [8]. It is well accepted now that COVID-19 is a very contagious disease and SARS-CoV-2 has the ability to spread through direct, indirect or close contact with an infected person, mainly through fluid droplets, which are expelled through sneezing, coughing or talking. The transmission may also occur by touching virus contaminated metal, paper or wood surfaces. Dry cough, fever, tiredness, whole body pain, headache, conjunctivitis, sore throat or diarrhoea are the common symptoms of this virus infection. In case of severe COVID-19 patients, epilepsy, excessive breathing problem, loss of movement may occur. In some cases, SARS-CoV-2 affected people may be asymptomatic and they may act as carriers and are primarily responsible for fast spreading of this virus in community. It has to be pointed out that the mortality rate by SARS-CoV-2 infection depends mainly with people with a history of diabetes, chronic lung disease, renal failure and cardiovascular issues.

Although, the process of vaccination is at full swing around all parts of the world, the number of infected patients is continuously increasing due to the ability of the virus to create new mutagenic strain at a rapid rate and at the same time, there are no specific drugs to combat this pandemic. Most of the currently available drugs for the treatment of viral infections belongs to antiviral, immune or anti-inflammatory therapy. Traditional medicines based on natural products are also the subject of growing interest in this context [9]. As mentioned earlier, because of viral mutations and the emergence of new viral strains [10], the effectiveness of conventional treatments of viral infections progressively fades away. Although the development of broad-spectrum antiviral drugs has attracted the attention of researchers and doctors[11], but their efficacy and side effects are not yet established and under the subject of extensive observation. Thus, multidisciplinary research efforts as well as study on statistical basis are required toward the development of alternative and effective antiviral therapies by targeting different phases of the replication cycle of the virus [12]. In this context, nanotechnology has gained considerable attention for the prevention as well as treatment of viral infections [13-14].

Nanoparticles and Drug delivery: Nanomaterials are less than one micrometre in size, falling in nano-regime and the size is comparable to the size of virus itself, thereby, allowing nanomaterials with effective functional qualities in combating it. The small size also provides a high surface-to-volume ratio, which in turn, enables the nanomaterials to be effective to play the role of delivery moieties, thereby, improving targeted drug delivery and gene modifications and allows accurate and fast virus detection. The application of nano-based technology in medical field is known as nanomedicine which deals with the use of nanomaterials for diagnosis, treatment, control and prevention of diseases [15-16]. The unique properties of nanoparticles such as small size, excellent solubility, adaptability and multifunctionality results in the development of better and safer drugs, tissue targeted treatments in recent times [17-18]. Nowadays, in pharmaceutical research and clinical settings, nano-particulate pharmaceutical drug delivery systems (NDD) are commonly used to increase the efficacy of medicines [19]. In addition, attempts have been made to develop multifunctional NDDs to react to various stimuli that are characteristic of the pathological location, by adding elements that respond to irregular pH, temperature and oxidation [17]. The interesting feature of multifunctional NDDs are that, they can respond to external ultrasound or magnetic fields.

Over the last few years, although a number of drugs with considerable lipophilicity are developed and marketed, but they suffer from one serious drawback – the low solubility in water, which in turn results in lower bioavailability and sub-optimal drug delivery. Nanoparticle-based formulations as well as lipid-based drug delivery systems are widely used in this context to increase the dissolution rate of these molecules [18-19]. This is quite understandable from the fact that drug encapsuled nanoparticles have a greater surface area, which, in turn, provide a higher coefficient of transfer of solution as compared to the mother drug counterpart.

Types of nanoparticles: Nanoparticles can be classified into four major categories: nanocrystalline, polymeric, nonpolymeric and lipid-based. A brief characteristic, sub classification and medical applications are hereby presented.

(a)Polymeric nanoparticles:

(i) Dendrimers: They consist of a structure of repeat branching chains, often adopt a spherical, symmetric three-dimensional morphology. Dendrimers have free end groups that can be easily swapped with biocompatible conjugate molecules [20], which can improve their limited cytotoxicity and permeability. The increased surface area facilitates the delivery of therapeutic agents to specific target sites.

(ii) Micelles: Micellar solutions are basically used to carry low-solubility therapeutic agents. The polymeric micelles are spherical in configuration, where the hydrophilic head groups surround the hydrophobic centres. The design of polymeric micelles enables to maintain their stability within physiological systems, thereby, make them an efficient therapeutic agent in drug delivery mechanism [21].

(iii) Protein nanoparticles: Protein nanoparticles, including viruses and virus-like particles are formed by recombinant activity. Protein polymers are self-assembled into usable drug delivery carriers by genetic modification, with polymer-based nanoparticle benefits [22]. Abraxane is a protein nanoparticle drug approved by the Food and Drug Administration (FDA).

(iv) Nanogels: Nanogels contain polymeric nonfluid network having dimension less than 100 nm and has the ability to swell in contact with a fluid. Nanogels have been used in various applications, including biochemical separation, cell culture, antitumor therapy and biosensors [23].

(b)Nonpolymeric nanoparticles:

(i)Carbon nanotubes: These are promising nonpolymeric transporters for therapeutic agents due to their size and stable geometric form [24]. Fullerenes are the most important members in this category and can serve as an effective antiviral, anticancer and antibiotic agents [25-26].

(ii) Nano diamonds: These are components of carbon-based nanoparticles having diameter less than 100 nm. Nano diamonds have special features, such as electrostatic surface properties as well as low chemically inert core cytotoxicity. Owing to their ability to immobilize various biomolecules, they are exceptional for medical applications such as magnetic resonance imaging (MRI) and drug delivery [27].

(iii) Metallic Nanoparticles: They are composed of gold, cobalt, nickel, iron and their respective oxides such as chromium dioxide, magnetite etc. They can be synthesised easily and allows modifications, which allows them to be encapsuled with different molecules, that include biological molecules such as DNA, proteins and peptides [28]. The significant parameter for their medicinal use is magnetic susceptibility. Superparamagnetic iron oxide nanoparticles are commonly used as contrast agents for MRI in hospitals. Gold nanoparticles are used extensively in the diagnosis and treatment in cancer due to lower cytotoxicity resulting from the inert nature of gold. Silica based nanoparticles provide significant advantages in nanomedicine due to their applicability to modelling complex structures and cost effectiveness. In addition, nanoparticles based on silica has the ability to interact with nucleic acids, allowing them to be used as targeted delivery vesicles [29].

(c) Lipid phase nanoparticles: Solid lipid nanoparticles are aqueous colloidal dispersions that contain a solid lipid matrix at room and body temperatures. Surfactants improve their stability, while the particular lipid used has the influence on the drug delivery characteristics. Liposomes, Exosomes are some important classes of lipid phase nanoparticles. They are important for a broad range of therapeutic uses, including tumour detection and treatment, antibacterial therapy and brain targeted drug delivery [30].

Nanotechnology to combat COVID-19:

From the forgoing discussions on the types and efficacy of nanoparticles in several medical crisis, nanotechnology is expected to hold a huge potential in the diagnosis, treatment and prevention of COVID-19. The approaches by which nanotechnology could help to fight against COVID-19 may be classified as their ability : (i) to design infection-proof personal protective equipment (PPE), particularly, to enhance the safety of frontline workers (ii) to develop effective anti-viral surface coatings, thus inactivate the virus, thereby preventing its spread (iii) to formulate highly sensitive nano-based sensors to quickly identify the immunological response (iv) to innovate new tissue targeted drugs having enhanced activity, minimum toxicity and sustained release (v) to develop a nano-based vaccination which can effectively boost cellular immune responses.

Disinfection of Surfaces: It is now a well-established fact that SARS-CoV-2 spread through micro-droplets emitted mainly from person to person or through touching contaminated surfaces [31]. Thus, contaminated surfaces in public places, such as hospitals, public transportation, schools, perks, large gathering in public meeting and holy places are the well-recognised common source for outbreaks of infection [32]. In this context, nanotechnology serves a lot of opportunities for the development of more efficient and promising disinfectant systems, by developing new materials for surfaces having antimicrobial activity with self-cleaning properties [33]. Some metallic nanoparticles, especially silver nanoparticles, may be used as a potent and broad-spectrum antiviral agent either with or without surface modifications [34]. Several nanomaterials (e.g., titanium dioxide, copper oxide and silver nanoparticles), when associated with polymers and textiles, can reduce the viability of viruses on surfaces, especially in conditions of light exposure [35]. Working in this direction a Chilean/USA-based company, Copper 3D, has developed a nanocomposite face mask named NanoHack in which 5% copper oxide nanoparticles are impregnated in three layers of nonwoven polypropylene filters, bestowing them with excellent antiviral activity against SARS-COV-2. This mask is popular around the world [36].

Besides several advantages, these systems suffer from the challenges in terms of issues like production costs, toxicity and environmental effects [37]. More extensive researches are going on the use of nanotechnology for more efficient disinfectant and sanitizing systems. [38-39].

Nanomaterials for PPE: To combat the spread of the coronavirus, the prime requirement is to use appropriate PPE as well as masks and gloves. Nanotechnology provides more comfortable, resistant and safer means for protection against biological and chemical risks [40-41], where some new functions like hydrophobicity, enhanced antimicrobial activity has been incorporated in facemasks, aprons, gloves, without affecting their basic texture. Their surfaces are modified by nanoscale biocides e.g., quaternary ammonium salts, polymers or peptides, which effectively controls microorganisms through oxidation of the microbial membrane [42]. The use of nanomaterials for facemasks protects against small particles of dimension less than 50 nm, whereas, N95/FEP2 facemasks can only protect against particles 100-300 nm in size. Besides, nanomaterials-based facemasks protection works as a filter plus microbicidal agent, resulting in blocking and killing or inactivating the pathogens. For gloves, use of silver nanoparticles has been reported [43].

Despite all these advantages, the side effects such as skin irritation, toxic effects in humans by the use of nanoparticles must also be properly investigated. Another point that should be taken into account that nanoparticles can be released from the clothes during washing, thereby depositing in the environment as waste.

Nanotechnology for virus detection and diagnosis: So far as the detection and diagnosis of COVID-19, the protein-based tests (serology) are considered to be a widely accepted method and are based on the presence of specific viral antigens or corresponding antibody responses of the immune system. The accuracy, reliability of these tests are limited by the possibility of cross-reactivity of the antibodies used or when a mutation occurs during the propagation period [43]. Nanotechnology under these circumstances provides an efficient and cost-effective tool for detection of SARS-CoV-2. Metallic and silica nanoparticles, carbon nanotubes are extensively used for virus detection [44]. In recent times, graphene-based nano biosensors [45] have contributed significantly in the process of detection of SARS-Cov-2 virus.

Nanotechnology based potential drug delivery systems to control viral infection: In practice, several drugs employed in the treatment of other diseases have been suggested worldwide as possible inhibitors of SARS-CoV-2; however, some of them can cause serious side effects or are still in the testing phase [46]. The mutating ability of the virus make some of the available drugs as ineffective. In addition, some drugs are affective only at high concentrations, which may cause toxicity in host cells. The use of nano-based formulations in this aspect has indicated a great potential for the control of viral infections, where nanoparticles can both enhance the efficacy of an antiviral drug and also reduce its toxicity [14]. In future, the use of nano-based antiviral therapies will be to target successfully the precise location of viral infection.

Nano vaccines: Recently, nanoparticles have caught attention as a promising approach to the development of a new generation of vaccines, since the nanoparticles can both serve as a carrier for the antigen and act as an adjuvant in many cases [47]. In addition, nano-based vaccines can protect antigens against premature degradation and provide sustained release, enhanced antigen stability, and provide targeted delivery of an immunogen. With the understanding of the interactions between nanoparticles and the immune system, it can be expected that nanotechnology will fare better in terms of delivering quicker, safer and more effective vaccines compared to those developed by conventional approaches.

Conclusion

Currently there are more questions than answers about SARS-CoV-2, as our knowledge is limited till now. Research addressing the cytology, epidemiology, mechanism of pathogenesis and detailed host immune response to the virus needs to work together to develop diagnostics, treatments and other control measures to combat the epidemic. One of the major challenges of nanotechnology-based application is to ensure the safe use of nanomaterials, since most of the studies have only evaluated the biocompatibility using in vitro approaches. Thus, reliable in vivo models are necessary to better understand the toxicokinetic behaviour of the nanoparticles in the body, especially for long-term exposure [48]. Another issue is the lack of standardized protocols for physicochemical and biological characterization of nanomaterials. Due to these limitations, generic protocols have been employed for characterization during the early stages of R&D, which explains the huge numbers of failures in terms of clinical translation of the final nano-based therapies [49]. To overcome the abovementioned hurdles, a closer collaboration between regulatory agencies, scientific experts in material science, pharmacology and toxicology is needed. Capacity for largescale manufacturing is another hurdle that needs to be overcome for broader commercialization of nano-based formulations. Furthermore, the characterization of protein corona is an essential step to be investigated in the process of nanomedicine development. In conclusion, according to the preceding discussions, nanotechnology serves as an important tool in the hand of virologists and researchers, for diagnostics, protection ,therapies and development of methodologists to fight against mild to severe viral infections; therefore, there is a good chance that, with more R&D, it will revolutionize the fight against COVID-19.

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References:

1. Zhou , P., Yang , XL., Wang XG et al.,2020, A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature ,579(7798) : 270–273.

2. Palestino, G., Silva, I.G ., Gonzalez-Ortega , O. and Rosales-Mendoza, S., 2020, Can nano-technology help in the fight against COVID-19? ´ Expert Rev., Anti Infect. Ther. , 18(9): 849–864.

3.WorldHealthOrganization.Timeline:WHO'sCOVID-19response. www.who.int/emergencies/diseases/novel-coronavirus-2019/interactive-timeline

4. Chen, N., Zhou, M., Dong X, X., Qu, J., Gong F, F., Han Y.et al., 2020, Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet., 395: 507–513.

5. Chauhan, G., Madou, M J, Kalra, S., Chopra, V., Ghosh, D. and Martinez-Chapa S O., 2020, Nanotechnology for COVID-19: therapeutics and vaccine research, ACS Nano, 14(7): 7760–7782.

6. Ruiz-Hitzky, E., Darder, M., Wicklein B. et al.,2020, Nanotechnology responses to COVID-19, Adv. Healthc. Mater., 9(19) : e2000979.

7. Liu, D X., Fung, T S., Chong, K K., Shukla, A. and Hilgenfeld, R., 2014, Accessory proteins of SARS-CoV and other coronaviruses,Antiviral Res., 109: 97–109.

8. Lukassen, S.,Chua,R L.,Trefzer T.et al., 2020, SARS-CoV-2 receptor ACE2 and TMPRSS2 are primarily expressed in bronchial transient secretory cells, J. EMBO , 39(10): e105114.

9. Kang, S., Peng, W., Zhu, Y., Lu, S., Zhou, M. and Lin W, W., 2020, Recent progress in understanding 2019 novel coronavirus (SARS-CoV-2) associated with human respiratory disease: detection, mechanisms and treatment, Int J Antimicrob Agents, 55: 105950.

10 Strasfeld, . L. and Chou. S., 2010, Antiviral drug resistance: mechanisms and clinical implications, Infect Dis Clin N Am., 24: 413–437.

11. Jackman, J.A., Lee, J. and Cho, N-J,2016, Nanomedicine for infectious disease applications: innovation towards broad-spectrum treatment of viral infections. 12: 1133–1139.

12. Mohammadi, P.P., Fakhri, S.,Asgary, S., Farzaei, MH. And Echeverría, J.,2019, The signaling pathways, and therapeutic targets of antiviral agents: focusing on the antiviral approaches and clinical perspectives of anthocyanins in the management of viral diseases, Front Pharmacol., 10: 1207.

13. Lembo, D., Donalisio, M., Civra A, A., Argenziano, M. and Cavalli , R.,2018, Nanomedicine formulations for the delivery of antiviral drugs: a promising solution for the treatment of viral infections, Expert Opin Drug Deliv,15: 93–114.

14. Singh, L., Kruger, H G., Maguire , G E M., Govender, T. and Parboosing, R., 2017, The role of nanotechnology in the treatment of viral infections, Ther Adv Infect Dis., 4: 105–131.

15. Cavalcanti, .I.D.L. and de-Cajuba, M.N.L.B, 2020, Pharmaceutical nanotechnology: which products are been designed against ´ COVID-19?, J. Nanopart. Res. , 22(9): 276.

16. Sahoo S.K., Parveen, S. and Panda, J.J. ,2007, The present and future of nanotechnology in human health care, Nanomedicine, : 3(1): 20–31.

17. Soares, S., Sousa, J., Pais, A. and Vitorino, C., 2018, Nanomedicine: principles, properties, and regulatory issues, Front Chem., 6: 360.

18. Fornaguera, C. and García-Celma, M.J., 2017 ,Personalized nanomedicine: a revolution at the nanoscale.,J Personal Med., 7: 12–20.

19. Narang, A.S. , Chang, R.K. and Hussain, M.A., 2013, Pharmaceutical development and regulatory considerations for nanoparticles and Approved nanoparticles for disease targeting and applications in COVID-19 nanoparticulate drug delivery systems, J Pharm Sci.,102(11) : 3867–3882.

20 Palmerston, . L.M. , Pan, J. and Torchilin, V.P., 2017, Dendrimers as nanocarriers for nucleic acid and drug delivery in cancer therapy, Molecules, 22(9): 1401.

21. Ahmad, Z., Shah, A., Siddiq, M., Kraatz, H-B, 2014, Polymeric micelles as drug delivery vehicles, RSC Adv., 4(33):17028–38.

22. Neek, M., Kim, T.L and Wang, S.W., 2019, Protein-based nanoparticles in cancer vaccine development, Nanomedicine, 15(1) : 164–174.

23. Sharma, A., Garg T, T., Aman, A., Panchal, K., Sharma, R. and Kumar, S. , 2016, Nanogel – An advanced drug delivery tool: current and future, Artif Cell Nanomed Biotechnol., 44(1): 165–177.

24. Reilly, R.M. , 2007, Carbon nanotubes: potential benefits and risks of nanotechnology in nuclear medicine. J Nucl Med., 48(7) : 1039–1042.

25. Tegos, G.P., Demidova, G.P. , Arcila-Lopez, D., Lee, H., Wharton , T., Gali, H., 2005, Cationic fullerenes are effective and selective antimicrobial photosensitizers, Chem Biol., 12(10) :1127–1135.

26. Bosi, S.,Da Ros, T., Castellano, S., Banfi, E. and Prato, M., 2000, Antimycobacterial activity of ionic fullerene derivatives. Bioorg Med Chem Lett. 10(10) : 1043–1045.

27. Chauhan, S., Jain, N. and Nagaich, U., 2020, Nanodiamonds with powerful ability for drug delivery and biomedical applications: recent updates on in vivo study and patents, J Pharm Anal. ,10(1) : 1–12.

28. Fan, C., Gao, W., Chen, Z. , Fan, H., Li, M. and Deng F, F., 2011,Tumor selectivity of stealth multi-functionalized superparamagnetic iron oxide nanoparticles, Int J Pharm., 404(1–2) : 180–190.

29. Bagheri, E., Ansari, L., Abnous , K., Taghdisi, S.M., Charbgoo, F. and Ramezani, M., 2018, Silica based hybrid materials for drug delivery and bioimaging, J Control Rel., 277 : 57–76.

30. Daraee, H., Etemadi, A., Kouhi, M., Alimirzalu, S. and Akbarzadeh, A., 2016, Application of liposomes in medicine and drug delivery, Artif Cell Nanomed Biotechnol. , 44(1) :381–391.

31. Herron, J.B.T., Hay-David, A.G.C., Gilliam, A.D. , Brennan, P.A., 2020, Personal protective equipment and Covid 19—a risk to healthcare staff? , Br J Oral Maxillofac Surg., 58(5): 500–502.

32 Kramer, .A. , Assadian, O., 2014, Survival of microorganisms on inanimate sur- faces. In: Use of biocidal surfaces for reduction of healthcare acquired infections, Springer International Publishing AG, 7–26.

33. Singh, L., Kruger, H.G. , Maguire, G.E.M. , Govender, T., Parboosing, R., 2017, The role of nanotechnology in the treatment of viral infections, Ther Adv Infect Dis., 4: 105–131.

34. Rai, M., Deshmukh, S.D., Ingle, A.P., Gupta, I.R., Galdiero, M., Galdiero, S., 2016,Metal nanoparticles: the protective nanoshield against virus infection, Crit Rev Microbiol., 42: 46–56.

35. Toledo G.G., Toledo,V.H. , Lanfredi AJC, A.J.C. , 2020, Promising nanostructured materials against enveloped virus, An. Acad. Bras. Cienc., 92(4): e20200718.

36.StatNano. Technology against COVID-19: nano insights into prevention, diagnosis and treatment – respiratory masks. https://statnano.com/technology-against-covid-19-nano-insights#Respiratory Masks.

37. Chan, W.C.W., 2020, Nano research for COVID-19, ACS Nano, 14: 3719–3720.

38. Huang, H., Fan, C. , Li, M., Nie, H-L, Wang, F-B, Wang H, H. et al., 2020, COVID-19: a call for physical scientists and engineers, ACS Nano., 14(4) : 3747–3754.

39. Campos, E.V.R., Pereira, A.E.S., de Oliveira, J.L., Carvalho, L.V., Casagrande, M.G., Lima, R.D., Fraceto, L.F., 2020, How can nanotechnology help to combat COVID-19? Opportunities and urgent need, J. Nanobiotechnol., 18: 1-25.

40.Conlon,M.A.,Facemask having one or more nanofber layers. 2014. https:// patents.google.com/patent/WO2014143039A1/en. Accessed 27 Apr 2020.

41.Lustenberger,F.,Nanofber fltering material for disposable/reusable respirators. 2016. https://patents.google.com/patent/US9446547B2/en. Accessed 27 Apr 2020. 89.

42. Mansi, A., Boccuni, F., Iavicoli, S., 2019, Nanomaterials as a new opportunity for protecting workers from biological risk, Ind Health, 57 : 668–675.

43. Spagnol ,C., Fragal ,E.H., Pereira, A.G.B., Nakamura,C.V., Muniz, E.C., Follmann, H.D.M.et al. , 2018, Cellulose nanowhiskers decorated with silver nanoparticles as an additive to antibacterial polymers membranes fabricated by electrospinning, J Colloid Interface Sci., 531 :705–715.

44. Draz, M.S., Shafee, H., 2018, Applications of gold nanoparticles in virus detection,Theranostics., 8 :1985–2017.

45. Seo, G., Lee, G., Kim, M. J., Baek, S-H, Choi M, M., Ku, K.B.et al., 2020, Rapid detection of COVID-19 causative virus (SARS-CoV-2) in Human nasopharyngeal swab specimens using field-effect transistor-based biosensor, ACS Nano., 14 :5135–5142.

46. Sanders, J.M., Monogue, M.L., Jodlowski, T.Z. and Cutrell, J.B. 2020, Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review, JAMA,323(18): 824–836.

47. Lung, P., Yang J, J.and Li, Q., 2020, Nanoparticle formulated vaccines: opportunities and challenges, Nanoscale., 12: 5746– 5763.

48. Beyth, N., Houri-Haddad, Y., Domb, A., Khan, W., Hazan, R., 2015, Alternative antimicrobial approach: nano-antimicrobial materials, Hindawi, 1 ; 246012.

49. , Ventola, C,L, 2017, Progress in nanomedicine: approved and investigational nanodrugs, Pharm Ther., 42:742–755.