Advanced Engineering Days

aed.mersin.edu.tr

Development in nanomaterials for prevention and treatment of COVID-19 and other viruses

Nagihan Emeksiz*[1], Selma Erat[1,2,3]

[1]*Mersin University, Institute of Science, Department of Nanotechnology and Advanced Materials, nagihanemeksiz@gmail.com*
[2]*Mersin University, Advanced Technology Education, Research and Application Center, Türkiye, selma.erat@mersin.edu.tr*
[3]*Mersin University, Vocational School of Technical Sciences, Medical Services and Techniques Department, Türkiye*

Cite this study: Emeksiz, N., & Erat, S. (2022). Development in nanomaterials for prevention and treatment of COVID-19 and other viruses. 3rd Advanced Engineering Days, 100-102

Keywords
Nanomaterials
COVID-19
Silver
Gold
Graphene oxide
Antiviral

Abstract

Nanotechnology is an exciting field that is studied by many different disciplines from industry to medicine. The improvement in nanotechnology is increasing day by day. The Coronavirus known as COVID-19 became most difficult health cries that affected the whole world. The World Health Organization reported the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a pandemic in 2020. Public health strategies such as isolation and quarantine have been formed to control the rapidly spreading pandemic. Metal nanoparticles (silver, coper, gold, boron, etc.) and carbon-based nanoparticle (graphene oxide) include antiviral and antibacterial activity by causing damage to the cell membranes of microorganisms. Recently, studies show that particularly, the nanomaterials are mostly preferred not only for antiviral effect but also for virus detection, drug delivery and vaccination. In this study, nanomaterials and their application in detection, prevention and treatment for COVID-19 are compared and discussed in detail.

Introduction

The materials, which have less than 100 nm in size at least in one dimension, are called nanomaterials. The surface area per unit cell increases once the size of the material decreases. Most atoms in a lattice are located on the surface or near the surface as a result of an increase in surface area. This case cause that the bonds between surface atoms become weak and high reactivity property ready for physical and chemical interaction [1]. Nanotechnology is used for improving the physical and biological properties of biomaterials, mainly in the field of drug delivery system, tissue engineering, bioimaging, stem cell research, diagnosis, and treatment of cancer.

The studies demonstrate antiviral activity of silver nanoparticles (Ag NPs). Ag NPs can inhibit a pathogenic virus in two different ways: either Ag nanoparticle binds to the virus surface protein and prevents it from binding to cell receptors or binds to the DNA or RNA of the virus so that it blocks the replication and reproduction of the virus in the host cells [2]. Lara et al. evaluated that antiviral effect of Ag NPs (30-50 nm) against HIV-1 (Human Immunodeficiency Virus) at non-cytotoxic concentrations using two different methods in vitro assays. The results show that the Ag NPs inhibit viral replication of HIV-1. Compared with the control (0.0 mg/mL), the interaction between glycoprotein (gp120) of HIV virus and cell receptor (CD4) decrease over 60% at the 5mg/mL Ag NPs. In addition, the Ag NPs retained their antiviral activity even 12 h after the HIV inoculation [3]. Chen et al. investigated that the antiviral activity of 0.6-9 nm graphene oxide (GO) nanosheets and GO nanosheets with 5-25 nm Ag NPs against enveloped (feline coronavirus) and non-enveloped (infectious bursal disease virus) viruses. Both GO nanosheets with Ag NPs and pure GO nanosheets exhibited antiviral activity against feline coronavirus (FCoV) [4]. Mori et al. searched the antiviral effect of chitosan (Ch) and Ag NPs composites of different sizes (3.5, 6.5 and 12.9 nm) against the H1N1 /Influenza A virus. As a result of the study, stronger antiviral activity has been observed in composites containing Ag NPs [5]. Jeremiah et al. evaluated the antiviral effect of Ag NPs of different concentrations. It was observed that the one with 10 nm size covered with PVP (polyvinylpyrrolidone) reduce the cytotoxicity effect and still inhibit extracellular SARS-CoV-2 [6]. Ghaffari et al. examined the antiviral activity of

zinc oxide nanoparticles (ZnO NPs) and PEG- ZnO NPs for H1N1 influenza virus. As shown in the TCID50 assay results, PEG- ZnO NPs exhibited antiviral effect on H1N1. However, there was not any decrease in H1N1 influenza virus at pre-exposure of cells to ZnO nanoparticles [7]. In another study, about the effect of metal nanoparticles on the HIV/AIDS virus, demonstrate that gold nanoparticles (Au NPs), which are stabilized with polyethylene glycol have antiviral effect on HIV virus by preventing CD4 dependent virion binding [8]. Nanoparticles are preferred to design smart drug delivery systems for controlled release behavior. In a study, Ag NPs was used as nanocarrier and the effect of Ag NPs against glycoproteins of COVID-19 virus. The SEM images showed that the damage of spike (S) glycoprotein and the protein membrane of COVID-19 virus after treatment with the Ag NPs/hydroxychloroquine (HQ, a known antiviral drug). In addition, TCID50 assay drug, which prepared 400 mg/ml of Ag NPs/HQ decrease the viability of COVID-19 virus to ~22% [9]. Uncontrolled spread of COVID-19 has caused the global health threat that has affected millions of people. Vaccination is the most effective health strategy in order to control and prevent the widespread of infectious diseases. The Moderna and Pfizer/BioNtech vaccines were designed using lipid nanoparticles for delivery mRNA, which codes the S glycoprotein of the COVID-19 virus surrounding by phospholipid membrane. When lipid-based vaccine is injected to host, the phospholipid membrane of the nanoparticle decomposes into host membrane and release the mRNA into the cytoplasm of the target cell. Then, host immune system is activated, and T-helper cells produce antibodies during recurrent attack of S glycoprotein on SARS-CoV-2 [10].

Material and Method

The particle size and shape of nanomaterials strongly depend on the synthesis techniques and preparation parameters (pH, temperature, duration times, etc.). Nanoparticles are produced by using physical (high energy ball milling, laser ablation, ion implantation, etc.), chemical (sol-gel, colloid), and biological (using biomolecule or plants) techniques [11]. Ag NPs were prepared by the green method. The phoenix dactylifera extract and Ag^+ solution was mixed by vigorous stirring at 60˚C for 15 min. [9]. Then, the resultant solution that was in clear red color was saved under 10˚C. Thereafter, Ag NPs were conjugated with the HQ. The prepared solution of Ag NPs and HQ was well mixed with stirring for 3h under ambient pressure and 40˚C and then resulted Ag NPs/HQ solution was stored under 10˚C [9].

GO nanosheets were prepared by using Hummers' method. Potassium manganate was added to graphite solution, including sodium nitrate and sulfuric acid. The obtained GO powders were dispersed in the silver-containing solution. According to pulse microwave-assisted (MA) synthesis, the GO-Ag solution was placed in the microwave according to supply the growth of silver seeds deposited on the GO surface. Finally, drying of the GO-Ag solution was completed inside a vacuum oven and the temperature was 60 ˚C [4].

Gold (III) chloride trihydrate ($HAuCl_4.3H_2O$), which dissolved in distilled water was blended with a magnetic stirrer until the gold solution was brought to boil. Sodium citrate dehydrate ($C_6H_5Na_3O_7.2H_2O$) which act reducing agent was dissolved in deionized water and then added to the gold solution. The mixture which was cooled overnight, filtered through a 0.2 µm membrane filter. The mixed solution of 17 nm Au NPs and PEG solution was centrifuged for 20 min. [8].

Chitosan solution was mixed with Ag NPs solution along with NaOH at room temperature, followed by stirring to precipitate the Ag NPs/Ch composite, and then the obtained Ag NPs/Ch composite was centrifuged for 10 min. [5].

Results

The Ag NPs and Au NPs efficiently blocked the fusion of HIV-1 viruses to the cell by interfering with gp120-CD4 interaction depending on the dose [3, 8]. Additionally, it was observed that the Ag NPs effectively inhibit extracellular SARS-CoV-2 to protect the target cells from infection [6]. After a time-of-addition experiment was performed, it was determined that Ag NPs retained their antiviral activity even 12 h after the HIV-1 inoculation [3]. The result shows that the Ag NPs intervene with the viral life cycle besides fusion or entry. The Au NPs were observed to be more effective than the Indinavir, which is a drug used as a component of highly active antiretroviral therapy [8]. The size and antiviral activity relation of Ag NPs was examined by using immunofluorescence analysis. Immunofluorescence imaging show that 100 nm Ag NPs had not antiviral an activity on SARS-CoV-2 virus. While 10 nm Ag NPs effected to SARS-CoV-2 virus [6].

By means of luminescent cell viability assay, the 50% cytotoxic concentration (CC_{50}) of the Ag NPs was determined as 3.9 ± 1.6 mg/mL, 1.11 ± 0.32 mg/mL, and 1.3 ± 0.58 mg/mL against HeLa-CD4-LTR-b-gal cells, human PBMC, and MT-2 cells, respectively [3]. The cell viability of The Hela-CD4-LTR-B-gal cell line defined after added Au NPs. The IC50 of Au NPs was found to be 1.12 ± 0.05 mg/ml [8]. Besides, the concentration of Ag NPs becomes cytotoxic to the cell lines Calu-3 (human lung epithelial cell) at 20 ppm and above [6].

The CC_{50} of GO and GO-Ag NPs in fcwf-4 cells was 17.4 mg/mL and 19.7 mg/mL, respectively [4]. The cytotoxicity of PEGylated ZnO NPs and ZnO NPs was measured as 75 µg/mL and 200 µg/mL, respectively. In contrast, it was observed that the antiviral activity of PEGylated ZnO NPs is greater than ZnO NPs [7].

Discussion

It was analyzed that the antiviral activity of nanocomposites enhanced by doping with Ag NPs. It was concluded that the Ag/Ch composite exhibited antiviral properties in all Ag NPs sizes while pure Ch did not have any antiviral effects. The GO nanosheets with Ag NPs exhibited antiviral activity for non-enveloped viruses even though viruses without envelopes are quite resistant to environmental stresses. However, the pure GO nanosheets could only inhibit the infection of the enveloped virus. Another point, there is a correlation between size of Ag NPs and antiviral activity.

Increasing the amount of nanometals in biomaterials leads to enhancing the antiviral effect. The cytotoxic effect on living cells may occurred by nanoparticle aggregation or using high dose of nanometals for strong antiviral activity. Nanometals are covered by polymers or doped with other biocompatibility materials to provide the immobilization of nanoparticles; thus, the cytotoxicity is decreased by preventing the release of unchecked ions (such as Ag^{+}, Zn^{+}). Regarding the studies aforementioned, we concluded that the Ag NPs/GO composites have less cytotoxic effect compared to polymer conjugated. One reason for that may be the strong immobilization of Ag NPs within the composites used.

The antiviral effect of Ag NPs on viruses is comprised of two ways: (1) The interaction of the virus before viral attachment to the host cell and (2) damaging viral surface protein in viral replication after infection of the host cell. The Au NPs have an antiviral mechanism similar to Ag NPs. The Au NPs prevent the attachment of glycoprotein found in virus to host cell receptors. The ZnO NPs inhibit viral life cycle, which occur after viral taken up by cells. However, the ZnO NPs are not able to prevent the host cell from the entry of viruses, unlike the Ag NPs and the Au NPs.

Conclusion

Nanotechnology is of interest to interdisciplinary researches due to the physical and chemical properties of nanomaterials. Some nanometal particles exhibit antimicrobial, anticancer, and anti-inflammatory activity. Therefore, biocompatible nanomaterials are used in the diagnosis and treatment of diseases. It was evaluated that the antiviral activity of nanomaterials (Ag, Au, ZnO, GO) even at non-cytotoxic dose. Nanomaterials can play a key role in the combat the COVID-19 pandemic or future global pandemics and/or diseases. For this reason, researches should focus on the enhancing the physical, chemical and/or biological properties of nanomaterials.

References

1. Vollath, D. (2013). Nanomaterials and nanocomposites, Nanomaterials, Wiley-VCH, 5-22.
2. Fauzi, B., Mahmoudi, E., Mohammad, A., Mustafa, N., Naomi, R., Salleh, A., Utami, N., (2020). The Potential of Silver Nanoparticles for Antiviral and Antibacterial Applications: A Mechanism of Action, Nanomaterials, 10, 1566.
3. Ayala-Nuñez, N., Ixtepan-Turrent, L., Lara, H., and Rodriguez-Padilla, C. (2010). Mode of antiviral action of silver nanoparticles against HIV-1, Journal of Nanobiotechnology, 8,1,1.
4. Chang, P., Chen, Y., Hsieh, C., Hsueh, Y., and Tzou, D. (2016). Antiviral Activity of Graphene–Silver Nanocomposites against Non-Enveloped and Enveloped Viruses. International Journal of Environmental Research and Public Health, 13,4,430.
5. Matsui, T., Miyahira, Y., Mori, Y., Nguyen, V., Q., Ishihara, M., and Ono, T., (2013). Antiviral activity of silver nanoparticle/chitosan composites against H1N1 influenza A virus, Nanoscale Research Letters, 8, 93.
6. Jeremiah, S., S., Miyakawa, K., Morita, T., Yamaoka, Y. (2020). Potent antiviral effect of silver nanoparticles on SARS-CoV-2, Biochemical and Biophysical Research Communications, 533,1, 195-200.
7. Ghaffari, H., Tavakoli, A., Moradi, A., Tabarraei, A., Bokharaei-Salim, F., Zahmatkeshan, M., Farahmand, M., Javanmard, D., Kiani, S., Esghaei, M., Pirhajati-Mahabadi, V., Monavari, S. and Ataei-Pirkooh, A., (2019). Inhibition of H1N1 influenza virus infection by zinc oxide nanoparticles: another emerging application of nanomedicine. Journal of Biomedical Science, 26,1.
8. Ganesan, S. and Vijayakumar, S. (2012). Gold Nanoparticles as an HIV Entry Inhibitor. Current HIV Research, 10, 8, 643-646.
9. Alheety, M., A., Ali, A., H., Alubaidy, M., H., and Dohare, S. (2022). Nano drug (AgNPs capped with hydroxychloroquine): Synthesis, characterization, anti-covid-19 and healing the wound infected with S. aureus. Materials Chemistry and Physics, 287.
10. De Soto, J., A. (2021). Evaluation of the Moderna, Pfizer/Biotech, Astrazeneca/Oxford and Sputnik V Vaccines for Covid-19, Advanced Research Journal of Medical and Clinical Sciences,7,1.
11. Çiftçi, H., Er Çalışkan, Ç., Öztürk, K., Yazıcı, B. (2021). Yeşil yöntemle sentezlenen biyoaktif nanopartiküller, Black Sea Journal of Engineering and Science, 4, 1.