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Nanomedicine in the Fight against Covid-19

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The coronavirus disease (Covid-19) caused by the SARS-CoV-2 virus has so far infected more than four million people worldwide, and the pandemic shows no signs of stopping. There is currently no known cure for Covid-19. According to the World Health Organization (WHO), the spread of Covid-19 can be controlled by a number of precautionary measures, including frequent handwashing, the spraying of surfaces or objects with disinfectants, and the wearing of face masks. The SARS-CoV-2 virus structure consists of spike proteins on the surface, membrane glycoproteins, small envelope proteins, nucleocapsid phosphoproteins and RNA. Many researchers and pharmaceutical companies around the world are focusing on this structure to develop a potential medical weapon to fight Covid-19. Nanomedicine – which refers to the application of nanotechnology to achieve innovation in healthcare – is proving important in this medical research. The use of nanomedicine in the fight against Covid-19 includes the design of nanotechnology-based masks, diagnostics devices, disinfectants, sanitisers, vaccines and drugs. According to Prof. Thomas Webster – a nanomedicine specialist at Northeastern University – the virus behind Covid-19 consists of a structure of a similar scale to nanoparticles, at a nanoscale of 1-100nm. Nanoparticles could attach to SARS-CoV-2 viruses and disrupt their structure, making it difficult for the virus to survive and reproduce in the body.

Potential contributions of nanomedicine in the fight against Covid-19

There are four areas where nanomedicine is making significant contributions in the fight against Covid-19: i) prevention (disinfection/sanitisation and personal protective equipment (PPE)), ii) screening and rapid diagnosis, iii) vaccine, and iv) treatment.

Disinfection/sanitisation

Nanotechnology-based antiviral disinfectants are highly effective virucidal agents against contagious viruses such as SARS-CoV-2. They can kill 99.9% of viruses on contaminated surfaces or objects, such as stainless steel, plastic, cardboard, aluminium, and many more. In the Czech Republic, scientists have tested two different nanotechnology-based disinfectants, made up of nanopolymers, for their effectiveness in fighting Covid-19. Both disinfectant products were tested on public transport, such as trams and buses, for the capability of long-term antibacterial and antiviral effects for about 21 days after application. These products could reduce the daily spraying of disinfectant agents, ultimately reducing costs. In the USA, New Jersey Hospital (NJH) used NanoVapor (FDA-approved, NanoVapor BioTech) as a disinfectant agent. NanoVapor is capable of killing SARS-CoV-2 on surfaces and objects in the hospital, and is effective for up to 70 days after application. NJH used this product as an additional measure to protect its staff and patients. Many other countries around the world are currently testing their own nanotechnology-based antiviral disinfectants and sanitisers for hand washing or to protect homes, hospitals and shoppers. These countries include Malaysia (Mydin Virus Nano Spray Buster/booth for the whole body disinfection) and the United Kingdom (MVX Protex antimicrobial coat spray, MVX Prime Ltd, UK), amongst others.

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Personal protective equipment (PPE)

Countries around the world are using face masks to prevent the spread of Covid-19. Surgical masks, N95 masks (fine dust masks) and/or other equivalent respirator-type masks are among those currently used by healthcare workers to protect themselves from coronavirus. However, these masks can only protect healthcare workers and/or individuals to a certain extent from respiratory secretions or viruses in the air. Nanotechnologies-based masks promise to offer unique solutions in the form of a new generation of face masks that are reusable, washable, recyclable, electrical and self-sterilised, while providing the wearer with the necessary protection against viruses. Nanotechnology-based masks have proved to

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be 99.9% efficient against coronavirus and other infection threats. Nanofiber masks are capable of trapping and killing viruses immediately upon contact. In a recent report, the Respilon Group – a Czech Republic nanofiber technology firm – claims to have developed a ReSpimask® face mask that is capable of trapping and killing viruses, including coronaviruses. ReSpimask® mask is made up of nanofiber technology with a three-layer membrane incorporated with copper dioxide (CuO) nanoparticles. In another report, the Hong Kong-based New World Development group claims to have developed self-sterilising nanodiamond-coated masks that are both affordable and highly effective against coronaviruses. Many other nanotechnology-based masks have been developed so far around the world, including electrical sterilisation breathing masks (Graphene mask, Guardian G-Volt^{Tm}, Belgium), nanotechnology-enabled N95 masks (nanofiber mask, Fanavaran Nano-Meghyas, Iran) and many others that are still in the development stages.

Screening and rapid diagnosis

The screening and rapid diagnosis of Covid-19 is crucial in preventing the spread of the disease in a community. Currently, the diagnostics of coronavirus are done by real-time reverse transcription-polymerase chain reaction (rRT-PCR) and GeneXpert. Although rRT-PCR is the gold standard for diagnosing coronavirus, and GeneXpert can offer rapid results in a short period of time, both are very complex, expensive, and lengthy – it can take 24 hours from sample collection to laboratory analysis to obtain diagnostic results. Rapid test kits are the fastest and cheapest way to test for SARS-CoV-2 in a short period of time; these include antibody tests and nanotechnology-based Covid-19 test kits/sensors.

Nanotechnology-based Covid-19 sensors are able to give results in less than 20 minutes. Rapid diagnostic kits such as these could reduce the burden on our current shortage of laboratory machines. For example, gold nanoparticles have been used by researchers in diagnostic RNA assays to detect amounts of coronavirus RNA sequences in a matter of minutes. The World Nano Foundation (WNF) claims to have identified a second generation rapid Covid-19 IgM/IgG antibody assay kit that consists of gold nanoparticles in the testing strip. This colloidal gold method has the capability of separating readings for IgM and IgG, detecting Covid-19 with more accuracy, and delivering results within 3-15 minutes. A recent article published by Norwegian SciTech News reported that researchers at the Norwegian University of Science and Technology (NTNU), in collaboration with St. Olavs Hospital, have developed iron oxide nanoparticles coated with silica as the next generation of coronavirus diagnostic tests. The advantage of using magnetic nanoparticles coated with silica in the testing kits is that these have a strong affinity for the coronavirus RNA that is extracted from the patient sample. In addition, these testing kits allow medical practitioners to conduct more than 30-40,000 tests in a day, and an estimated 150,000 Covid-19 tests per week. Furthermore, nanotechnology-based diagnostic devices are capable of measuring and interacting with single biological events, which means they have the capability of diagnosing single cells or viruses within a patient sample with a very low viral titre, which is very difficult to do when using conventional methods such as rRT-PCR, GeneXpert or Covid-19 antibody test (ELISA).

Vaccine and cure

There is currently no vaccine or cure for Covid-19. Several Covid-19 vaccines and treatments are in development and clinical trial phases, including nanotechnology-based vaccines and therapies. Conventional vaccines and/or DNA vaccines show promise for a universal influenza vaccine, but they have several downfalls, including the failure to engage the immune system, and their high toxicity and low stability in vivo. It is very difficult to deliver them to target areas, and they are easily eliminated in the reticuloendothelial system (RES). Nanovaccines, which are a new generation of vaccines that utilise nanoparticles (NPs), offer a safe delivery vehicle to a target site. Nanosized particles include liposomes, protein, polymeric nanoparticles and nanospheres. Nanovaccines can improve the efficiency of vaccine delivery, can offer prolonged protection, and can induce both humoral and cell-mediated immune responses. One example of this is self-assembling ferritin proteins that formed nanoparticles, which can promote the production of antibodies to neutralize viruses, including coronaviruses. Nanovaccines that are currently undergoing clinical trials include the mRNA-1273 vaccine (Phase 1 trial, Moderna, USA), NVX-CoV2373 (a nanovaccine that is a recombinant protein nanoparticle technology platform; Novavax Inc, USA), BNT162 DNA vaccine (Phase I/II trials) developed by Pfizer (New York City, USA), in collaboration with BioNTech (Mainz, Germany), INO-4800 DNA vaccine, in Phase I clinical trial (Inovio Pharmaceuticals, USA), Ad5-nCoV vaccine (a recombinant novel coronavirus vaccine; Cansino Biologics Inc, Tianjin, China), and INO-4800 DNA vaccine (Phase I/II trials) developed by Korea National Institute of Health (Osong, Republic of Korea), in collaboration with the International Vaccine Institute (Seoul, South Korea). N4 Pharma Plc (United Kingdom) recently announced Nuvec® technology, a silica nanoparticle with elongated silica spikes radiating from the core. On the other hand, Alnylam Pharmaceuticals has synthesized more than 350 siRNAs targeting all available genomes of coranoviruses in the USA, using RNA interference (RNAi) therapy. A collaborative study between Northwestern University and Massachusetts Institute of Technology claims to have discovered a peptide molecule that binds strongly and specifically to the spike proteins on the surface of SARS-CoV-2. The peptide molecule is encapsulated within the nanostructure to protect it from elimination in the RES, and is delivered into the target site where there are coronaviruses. Nanomedicine studies also provide insights into anti-malaria chloroquine's efficacy against Covid-19. Synthetic nanoparticles were allowed to interact with host cells in the presence of chloroquine, *in vitro*. The studies provide clues on chloroquine-induced alterations of Covid-19 cellular uptake. Although cell culture studies have proved that chloroquine might have antiviral activity against Covid-19, further studies or positive clinical trial results are still required.

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Conclusion

Nanotechnology-based antiviral disinfectants are highly effective and could be used in South Africa for increased surface disinfection or sanitisation in public transport, hospitals, schools, supermarkets and homes. They could also be applied once a month instead of on a daily basis, which is the case with conventional disinfectant agents. In the case of PPE, nanotechnologies promise to offer a new generation of face masks that are reusable, washable, recyclable, and self-sterilised, as well as capable of killing the virus immediately upon contact. In the case of Covid-19 diagnostics, nanotechnology promises to offer cheap and quick Covid-19 tests that deliver accurate results in less than 20 minutes. When it comes to Covid-19 treatments and vaccine, nanomedicine promises to offer nano-enabled medicine products that are capable of neutralising viruses. There are currently many organisations around the world that are busy working on the development of nanovaccines and treatments, some of which are currently undergoing clinical trials. However, extensive research is still required in order to declare the success of nanomedicine in the fight against the Covid-19 outbreak, as there still exist questions concerning the efficacy and side effects of nanotechnology-based vaccines and treatments on humans, as well as the environmental impact of nanomaterials. ■

References

Chard, L. (2020). News updates: nano-based vaccines for treatment of COVID-19. [online] The Nanomed Zone. Available at: https://www.nanomedzone.com/covid-19-updates-nano-based-vaccines-for-treatment-of-covid-19/ [Accessed 29 Apr. 2020]

StatNano, (2020). Nanotechnology in battle against coronavirus. [online] Available at: https://statnano.com/nanotechnology-in-battle-against-coronavirus [Accessed 30 Apr. 2020]