Game Changing Solutions for Pharmaceutical Industries: In Relevance to Covid-19

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Abstract

To combat the coronavirus pandemic, various early diagnostic tools and kits have been developed. The design, development, and application of technologies are affected by the pandemic. A deeper comprehension of the roles that technology and diagnostic tools play in early diagnosis is urgently needed. The molecular technologies that are being developed to counteract COVID-19's risks are examined in this study along with pertinent problems with technology development, design, and application. It also offers viewpoints and recommendations on how experts in information systems and technology might contribute to the fight against the COVID-19 pandemic. With the help of this study, future research and the development of biosensor technology could be encouraged, leading to improved ways to combat the COVID-19 pandemic and other pandemics in the future.

Keywords: *Coronavirus; diagnostic tools; technology development; biosensor technology;*

Introduction

The Coronavirus Disease Pandemic is a COVID-19-related severe acute respiratory syndrome coronavirus 2 outbreak that is still going on around the world (SARS-CoV-2). In Wuhan, China, it was first discovered in December 2019. On January 20, 2020, and March 11, 2020, respectively, the World Health Organization labelled the outbreak a pandemic and a public health emergency of international concern. One of the deadliest pandemics in history, COVID-19 had more than 128 million confirmed cases as of 30 March 2021 and was responsible for more than 2.8 million deaths. WHO reports that as of March 28, 2021, there were roughly 126,359,540 confirmed cases, including 2,769,473 fatalities (1). Combating COVID-19 and upcoming pandemics is a crucial task.

Positive-sense single-stranded RNA virus with an envelope is known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Three different types of proteins-spike (S), envelope (E), and membrane (M) proteins-make up the majority of the SARS-CoV-2 envelope. Respiratory droplets are the main method of viral transmission2. The S proteins on

the SARS-CoV-2 virus envelope bind to the angiotensin converting enzyme 2 (ACE2) receptor on host epithelial cells as the virus particles enter respiratory tracts, promoting virus infection and replication and causing pneumonia symptoms like fever, cough, fatigue, and shortness of breath3.

The COVID-19 pandemic has caused a huge effect on hospital systems, businesses, schools, and the economy. It becomes crucial for society to use telemedicine, telework, and online education to stop the coronavirus from spreading. Due to the pandemic, there is an urgent need for initiatives to deploy cutting-edge technologies to mitigate the effects of COVID-19 on our way of life. 4. Researchers and scientists throughout the world are under tremendous pressure to create a vaccine and early diagnostic tools to battle the Covid-19 pandemic as a result of the continued worst scenarios produced by this pandemic. The epidemic has boosted prospects for technological advancement and given scholars a once-in-a-lifetime opportunity to examine the research and use of technology, including information management, work procedures, and the design and usage of technologies.

Challenges during Pandemic

Since the pandemic's announcement, fundamental services like routine medical treatment and others have been disrupted or have more limited access. In various nations, hospital services have been reorganised with temporary care. Due to the risk of infection, some hospitals have been unable to admit new inpatients. Researchers and scientists from all over the world were under a great deal of pressure to create novel vaccines, treatments, and early diagnostic tools during this crisis. The COVID-19 pandemic has had a significant impact on research activities, including various difficulties for clinical and surgical trainees. All research initiatives and clinical trials unconnected to COVID-19 came to an end as a direct result of lockdown measures and the closure of the majority of university research centres. A significant number of clinical academics have returned to full-time clinical responsibilities as a result of changes. Since March 2020, it has been extremely difficult to conduct clinical research as a result of the suspension of numerous healthcare services. The immediate and lasting effects of COVID-19 on clinical studies were evident. All clinical trials but those concentrating on COVID-19 have been stopped. The possibility of COVID-19 spreading has also caused the suspension of new study enrolment. Clinical trials that are currently underway and those that will be conducted in the future have, if possible, been modified to allow for the use of virtual monitoring systems to reduce the risk of infection among participants[5]. The quick adoption of telemedicine, telework, and online education in response to the coronavirus danger serves as a reminder of the many advantages of digital technology and how it may be used to manage and lower the risks associated with the lockdown both during and after the pandemic. It is common knowledge that technology plays a significant role in risk management, clinical decision support, and healthcare.

Existing diagnostic tools

The FDA of the United States is actively involved in accepting submissions and granting approvals for many of the vaccines and medications that are currently undergoing research and development (R and D) to address the current SARS-CoV-2 pandemic crisis. Despite the fact that the development of vaccines and therapeutics is progressing at a rapid rate. Early detection

and thorough contact tracing, as carried out by South Korean authorities, have been identified as key strategies for halting the spread of SARS-CoV-2 infections[6].

Patients with SARS-CoV-2 have symptoms that are typical of pneumonia-like conditions and cannot be used to make a precise diagnosis. According to reports, 44% of the 1099 SARS-CoV-2 patients from China who had been surveyed at the start of the disease's dissemination had moderate fever-like symptoms prior to hospital admission, but more than 80% of the patients who had been confirmed had fever-like symptoms by the time they were admitted. Real-time reverse transcription polymerase chain reaction (RT-PCR) and primarily CT scans were used as the major diagnostics for screening and detecting SARS-CoV-2 infections prior to the development of nucleic acid-based testing kits.

Nucleic acid-based diagnostics for SARS-CoV-2

The SARS-CoV-2 patients were rapidly identified using a variety of RT-PCR assays. In the RT-PCR technique, the isolated RNA materials are reverse-transcribed into complementary DNA strands (c-DNA), and the resulting copies of the c-DNA are amplified (7,8). The RT-PCR approach, often regarded as a gold standard protocol in the confirmation of SARS-CoV-2 infections, depends on the ability to amplify a modest concentration of viral nucleic acid components collected in test vials. Reverse transcriptase reacts with viral RNA to convert it into c-DNA, which is the first step in the RT-PCR procedure (RNA-dependent DNA polymerase). Currently, swab test samples that are commonly taken from the upper respiratory tracts are required for RT-PCR tests established for the diagnosis of SARS-CoV-2 patients.

Computed tomographic scans for SARS-CoV-2

With reverse transcriptase (RNA- Due to the lack of RT-PCR kits at the time of the outbreak, limited testing facilities, and potential for false-negative results, healthcare staff were advised to use chest CT scans for clinical evaluation of the severity of SARS-CoV-2 infections9. A thorough pathophysiology report from a chest CT scan can be helpful in determining the severity of illness evolution and identification 10.

Emerging diagnostics for SARS-CoV-2

The most common tests used to confirm patients who are suspected at this time are a chest CT scan, some blood testing parameters, and RNA detection of SARS-CoV-2 in BAL and nasopharyngeal swab samples11. Real-time quantitative PCR (RT-qPCR) can be used in accredited test facilities under biohazard safety class II to identify any reported viral nucleic acids. However, RT-qPCR test kits are known to occasionally produce false-positive or false-negative results; as a result, they must follow a swab sampling procedure and RNA extraction protocol. Additionally, there is a chance that the virus, even though it is present in the patient, may not be visible within the nose-pharynx mucous membrane11. Recently, certain assertions have been made regarding a disparity between the diagnostic effectiveness of CT and RT-qPCR, the latter having been discovered.

Reverse-transcription loop-mediated isothermal-amplification (RT- LAMP)

In order to diagnose SARS-CoV-2 infection, nucleic acid-based testing with isothermal amplification is currently being prepared due to its high diagnostic accuracy. This approach, unlike RT-PCR12, is conducted at a predetermined temperature and does not require expensive or specialised laboratory setups to achieve great analytical sensitivity. The method uses either RPA, also known as a loop-mediated isothermal-amplification, or helicase-dependent amplification (LAMP). Several institutes are currently successfully researching and developing reverse transcription and LAMP technology (RT-LAMP), which has also undergone clinical evaluation for its accuracy, speed, and POC diagnosis service for SARS-CoV-2 suspected patients. 4,9,10. Reverse transcription (RT-LAMP) has also been put through clinical testing The test samples in the tube are used in RT-LAMP diagnostic tests to amplify the target DNA strands that would otherwise be detected using a variety of methods, including colorimetric reactions, pH-sensitive dyes, or fluorescence assays using a fluorescent dye that specifically binds to the c-DNA strands13. The RT-LAMP assay can be finished in one hour at 60–65 °C and has an analytical sensitivity that is within the limit of detection of 70–75 copies/L in the test samples.

Isothermal amplification combined with CRISPR technology

The key feature of CRISPR-based detection technologies that needs to be emphasised is that, if the sequences are correct, isothermal amplification of the products produces signals, which offers higher analytical specificity than that of using pH indicators or fluorescent dyes due to their non-specificity14. This technique successfully detected 10 copies of RNA per microliter of SARS-CoV-2 RNA extract; both amplification and detection were completed in less than 30 minutes of incubation; it was indicated that this technique could be helpful for on-site analysis and point-of-care testing.

Emerging serological tests for SARS-CoV-2

In order to: (a) track down suspect contacts; (b) encourage serological surveillance at the national, regional, and local levels; and (c) classify those who might have already passed infection asymptomatically[15], it is crucial at this time to perform serological tests that look for SARS-CoV-2 specific antibodies in the patient's blood. The S protein of SARS-CoV-2 has been shown to have a substantial role in the contact, fusion, and intracellular entrance of the virus and host cells. As a result, it is a key target for the creation of antibodies, cellular entry inhibitors, and vaccines. Furthermore, different serological tests can be designed and used retroactively for autopsy diagnosis purposes. These techniques can also be successfully combined with recently developed molecular tests due to their improved diagnostic accuracy. Additionally, in the future, serological diagnostic tests may significantly contribute to enhancing the effectiveness of the assessment of any licenced vaccines[16]. Lack of unique antibodies for each and every SARS-CoV-2 protein has emerged as the primary obstacle to the development of diagnostic instruments that can effectively identify minuscule quantities of viral proteins.[17].

Viral antigens and antibodies produced by the immune system in response to viral infections are both included in viral protein-based diagnosis, which makes it useful for diagnosing SARS-

CoV-2 infections. However, because to variations in viral such protein concentrations, changes in viral-load over the SARS-CoV-2 infection time-course may make the diagnosis for these approaches hard. Particularly during the first week of illness and the beginning of severe symptoms, salivary samples show high viral loads; nevertheless, such viral load scenarios can gradually diminish during the duration of infection18 (To et al., 2020). For post-infection surveillance strategies used to control the SARS-CoV-2 crisis, antibody-based protein assays are known to be helpful. As a result, there is a larger window of opportunity for post-infection detection and precise data gathering. On the other hand, antibodies build in response to SARS-CoV-2 infections. The likelihood of encountering cross-reactivity between those antibodies produced in response to the SARS-CoV-2 infections and also to those formed in response to other types of coronaviruses poses potential difficulties for the development of such diagnosis for high throughput screening and accurate serological diagnosis. The S protein in plasma samples taken from fully recovered SARS-CoV-2 patients has been shown to frequently cross-react with both SARS-CoV and SARS-CoV-2 as well as with several other coronaviruses.

Point-of-care services

Protein test kits, nucleic acid molecular diagnostic kits, and testing at POC service centres are the main areas of SARS-CoV-2 diagnostic research that is urgently being established. Integration of various tests into multiplex panel systems should also be given substantial consideration as a long-term priority19. In order to enhance monitoring efforts, serological tests utilising protein-based test kits are increasingly being used alongside nucleic acid-based test kits. In contrast to nucleic acid-based test kits, which are limited in their ability to detect patients who have already recovered, protein-based diagnostic tests can identify asymptomatic infections after a patient has fully recovered. Thus, protein-based test kits may enable doctors to screen and contact-trace both sick and recovered patients, increasing the likelihood that the total number of SARS-CoV-2-infected people can be estimated. According to research on POC in cancer detection20, POC service centres can make testing SARS-CoV-2 infections more affordable and portable. They also enable the diagnosis of patients far from centralised facility centres in urban community health centres, which lessens the stress on clinicians. POC tests enable the diagnosis of suspect and infected persons without requiring the transportation of their test samples to the central facilities, enabling the detection of SARS-CoV-2-infected patients at neighbourhood community centres without the need for complex laboratory facilities. The development of a lateral flow SARS-CoV-2 antigen assay for point-of-care (POC) identification of infected patients21,21. A microfluidic device-based technique is a significant alternative that can be taken into account for a POC system. These gadgets use a tiny chip that has reaction cavities and micrometer-wide channels engraved on it. Glass, poly-dimethyl sulfoxide, and functionalized paper are common materials that are used to make the chips in order to separate and combine some liquid samples utilising a mechanism of capillary, vacuum, or electro-kinetic forces.

The microfluidic system's primary advantages include the requirement for a small sample volume, quick diagnosis, compactness, and superior portability22. The detection of biomarkers, amplification, sample preparation, and fluid handling must be made simpler using microfluidic platforms in order to accomplish POC diagnostics and high-throughput multiplexing.

Limitation and challenges

The SARS-CoV-2 RNA can be quickly and accurately detected using molecular diagnostics, which are also often quantitative. They are, however, difficult, expensive, and delayed to deliver. A single RT-PCR test kit may cost more than $100, while establishing a diagnostic/processing facility would cost more than $15,000 and take more than 24 hours to complete from the time the sample is taken to the time the results are available. The molecular diagnostics are also not meant for end users and are only for medium- or high-complexity laboratories and qualified clinical laboratory workers.

Current biosensor techniques for SARS-CoV-2 detection

A biosensor is a type of analytical device that combines a biological component and a transducer. In addition to the clinically accepted methods used for diagnostics in hospitals, a number of biosensor-based technologies are being developed and some are already in use to diagnose COVID-19 pneumonia. Current diagnostic methods and potential biosensing platforms for COVID-19, include I COVID-19 patients, (ii) sample methodologies, (iii) biomarkers and indicators, (iv) diagnostic approaches, and (v) prospective biosensors. In order to diagnose COVID-19 patients with mild to severe symptoms and assess the effectiveness of anti-inflammation therapies, biosensors with the ability to continuously monitor biomarkers would be possible choices. The best alternative instruments are biosensors because they have the potential to be operated with smartphones and exhibit quick reaction, high accuracy, greater sensitivity, and early detection capabilities. Fluorescence-based biosensors, colorimetric, localised surface plasmon resonance (LSPR), surface enhanced raman scattering (SERS), quartz crystal microbalance (QCM), field-effect transistor (FET)-based, and electrochemical (EC) biosensors are some of the different types of biosensors being developed or used for the diagnosis of the COVID-19 pandemic.[23]

FET-based Biosensing

Field-effect transistor (FET)-based biosensing devices have numerous prospective advantages compared to currently available diagnostic methods, including the capacity to be extremely sensitive and to instantly detect small volumes of target analyte. These biosensors could be used for point-of-care tests, clinical analysis, and on-site diagnostics. Due to its capacity to detect adjacent surface fluctuations and serve as an ideal sensing platform, graphene, which has hexagonal carbon atoms exposed on its surface and is electronically conductive, high charge mobility, and specific surface area, has proven to be extremely sensitive in sensing systems. As a result, biosensors are becoming a popular option for detecting different virus types, but they still have significant limitations. Graphene being a nanomaterial, to produce graphene with similar specifications is challenging and if any of the parameters vary then the response characteristic of the sensor may change. Controlling the virus's ability to bind to an antibody can occasionally be challenging**.**

Conclusions and future outlooks

For the early stage detection of SARS-CoV-2 so that these life threatening infections can be diagnosed in the early stages, a cost-effective and repeatable miniaturised GFET sensor with

the potential for dependable virus diagnostics with high sensitivity and selectivity is required. In the future, biosensor approaches will be the most effective technology for achieving the objectives of early disease diagnosis.

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