



Sustainable materials and COVID-19 detection biosensor: A brief review

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ABSTRACT

COVID-19 is the current global problem. Billions of infected cases due to the pandemic cause an emergency requirement to contain the pandemic. A basic concept to manage the outbreak is an early diagnosis and prompt treatment. To diagnose COVID-19, the new biosensors become new interventions that are hopeful to help effective diagnosis. In clinical material science, the issues on materials of COVID-19 detection biosensor is very interesting. In this brief review, the authors summarize and discuss on sustainable materials and COVID-19 detection biosensor. The paper, cellulose and graphene - based materials are specifically focused and biosensors for RNA sensing, antigenic determination and immune response detection are covered in this short article.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a new emerging contagious disease caused by the coronavirus 2 that causes severe acute respiratory syndrome. In December of 2019, the first known case was discovered in East Asia. Since then, the disease has spread worldwide, resulting in a pandemic [1]. COVID-19 is an acute respiratory tract infection. Fever, cough, headache, weariness, breathing difficulty, loss of smell, and loss of taste are common symptoms of COVID-19. Symptoms might appear anywhere from one to fourteen days after being exposed to the virus [2–8]. At least one-third of those who are afflicted do not show any signs or symptoms. The majority of people who acquire symptoms significant enough to be classified as patients have mild to moderate symptoms (up to mild pneumonia), whereas few per centage of cases have severe symptoms (dyspnea, hypoxia, or more than 50% lung involvement) [2–8]. People who are older are more likely to experience severe symptoms. Some persons continue to have a variety of symptoms (long COVID) months after recovery, and organ damage has been reported. Long-term researches are being conducted to learn more about the disease's long-term impact [2–8].

COVID-19 is the current global issue. The pandemic's billions of infected cases demand an immediate reaction to keep the epidemic under control. Early detection and treatment are critical for containing the

outbreak. COVID 19 can be identified based on symptoms and then validated by reverse transcription polymerase chain reaction (RT-PCR) or other nucleic acid testing of contaminated secretions [6]. Chest computerized tomography (CT) scans, in addition to laboratory tests, may be useful in diagnosing COVID 19 in people who have a high clinical suspicion of infection [6]. Serological tests, which identify antibodies produced by the body in response to infection, can be used to diagnose a previous infection [2–8]. The new biosensors are being used to diagnose COVID-19, and they are hoped to aid in accurate diagnosis. The difficulties surrounding materials for COVID-19 detection biosensors are extremely interesting in clinical material science.

Although there are various studies on innovative biosensors for COVID-19 diagnosis, there are few reports on biosensors based on sustainable materials. Furthermore, there is a scarcity of data on systematic reviews for sustainable materials-based biosensors. The current paper presents an overview of this topic based on a systematic review. The majority of earlier articles have focused solely on the biosensor's material science features, such as production technique and characteristics. The connection to real-world clinical application is just briefly mentioned. The current study adds to the issue about the exact effectiveness of the sensing system in real clinical use of the sustainable materials – based biosensor. Conceptually, a biosensor might be made of a very good material and have good analytical performance, but it might be useless if it is

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not applicable to serve the real clinical need. The point of view on material and sensor selection based on clinical data is also innovative in this article.

The authors describe and discuss sustainable materials and the COVID-19 detecting biosensor in this brief review. This short article focuses on paper, cellulose, and graphene-based materials, as well as biosensors for RNA sensing, antigenic identification, and immune response monitoring for application in COVID-19 diagnosis. Details of available sustainable materials and specific application in the COVID-19 diagnostic system are presented and discussed.

2. Biosensor and diagnosis of COVID-19

As already mentioned, the diagnosis of COVID-19 is very important for success in disease control. One of the cornerstones of pandemic control is a rapid and reliable laboratory detection of active COVID-19 infection. With so many tests on the market, non-specialists may find it difficult to apply the suitable specimen type and laboratory-testing technique in the relevant clinical circumstance [9]. The differences in diagnostic performance between upper and lower respiratory tract specimens, as well as the role of blood and fecal specimens are reported [9]. Because there have been clinically recorded cases of asymptomatic SARS-CoV-2 carriers, early and precise diagnosis is critical for disease control and prevention. Both RT-PCR and CT tests would boost sensitivity and quarantine efficacy when used together, something neither could do alone [10,11]. Many of the technologies and techniques used to diagnose COVID-19, as well as the methodologies established by various research institutes and commercial devices and kits made by corporations for the detection of SARS-CoV-2, differ in their clinical utility. Following a discussion of the present approaches, advantages and limitations are highlighted [11].

The pandemic has quickly spread over the globe. Despite significant attempts to restrict the disease, the virus continues to be prevalent in a number of nations, with various degrees of clinical symptoms. A joint approach comprising correct diagnosis, epidemiology, surveillance, and prophylaxis is required to contain this pandemic [6]. Proper diagnosis using quick technology, on the other hand, is critical [10–12]. With the rising number of COVID-19 cases, precise and timely identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is critical for efficient COVID-19 prevention and management, as well as limiting the virus's spread. The RT-PCR assay is regarded the gold standard for early virus identification, but due to its technical complexity, it has limited use as a bedside diagnostic [12]. To address these issues, many point-of-care (POC) tests have been developed to help with COVID-19 diagnosis outside of centralized testing laboratories and to speed up clinical decision-making with the shortest possible turnaround time [12]. Rapid antigen or antibody testing, immunoenzymatic serological tests, and RT-PCR-based molecular assays are the most frequently used and validated procedures now available [6]. Other techniques, such as isothermal nucleic acid amplification, clusters of regularly interspaced short palindromic repeats/Cas (CRISPR/Cas)-based approaches, or digital PCR methods, are now being employed in research settings or are pending authorisation for diagnostic use by competent authorities [13].

Newer, more efficient approaches for the quick detection of viral analyses are needed, taking into account viruses' flexibility and reproduction habitats. These methodologies must be implemented in a way that ensures greater accuracy, portability, and large-scale availability to test a big population [14]. There is a lot of interest in developing new COVID-19 biosensors that are fast, reliable, and sensitive. These biosensors would be a single-step identification or sensing approach that would avoid separation (nucleic acid extraction), incubation, and the need of any signal-reporting agents. COVID-19 biosensors are primarily based on surface nucleoproteins that attach to the host angiotensin-converting enzyme 2 (ACE-2) receptor and internal genetic material; they are highly selective [14]. The detection of biomarkers from human hosts other than antibodies or immunoglobulins could be a strategy for building novel COVID-19 biosensors [14].

3. Sustainable materials and COVID-19 detection biosensor

The COVID-19 pandemic exposed fundamental flaws in the current infectious disease diagnostic serology approach, which relies on sophisticated test workflows, laboratory-based gear, and expensive materials for sample and reagent management [6]. Longer wait times for test results, the expensive cost of gold-standard PCR tests, and the low sensitivity of rapid point-of-care tests all contributed to society's failure to quickly identify COVID-19-positive persons for quarantine, which has hampered the economy's restoration to normal operations [6]. The expense and time necessary to build single-use disposable microfluidic plastic cartridges fabricated by injection molding continues to stymie the widespread commercial availability of new test kits. However, the current concept tends towards the use of green sustainable materials that is the solution for in waste management.

Sustainable materials are the current concept and it is also concordant with the present trend of green and environmental friendly technology [15,16]. Many legislative initiatives try to address a material's or product's safety and sustainability early in the design process, rather than depending on controls and procedures to limit their impact on human health and the environment after the fact [15,16]. Biodegradable materials have recently emerged, presenting a great possibility to change healthcare technologies by allowing sensors to disintegrate naturally after usage [15]. Eco-friendly sensor systems made of biodegradable materials may also help to address some of the world's most pressing environmental challenges by lowering the amount of electronic or medical waste created and, as a result, the carbon footprint [15]. Basically, sustainable materials are materials used throughout our consumer and industrial economies that can be produced in sufficient quantities without depleting non-renewable resources or upsetting the environment's and critical natural resource systems' established steady-state balance [15,16]. Examples of currently widely used sustainable materials are paper, cellulose and graphene (Table 1). The biosensors are employed for early detection and serve a critical role in avoiding disease progression across the body. Because paper and paper-like materials are cheap, abundant, and degradable, there has recently been a popular demand to employ them for POC testing devices (e.g. nitrocellulose membrane) [16]. Microfluidic paper-based analytical devices are extremely promising since they are cost-effective, simple to use, rapid, precise, and long-lasting in a variety of environments [16].

Because of their complexity and dynamic behavior, smart nanomaterials and enabled goods may provide new issues for safety and sustainability assessment. Furthermore, present regulatory structures, particularly in the European Union, are likely insufficient to deal with them [17]. What is currently lacking is a systematic and complete strategy that allows for the early consideration of sustainability and safety factors in the material design stage [17]. Green chemistry concepts can be used to make nanomaterials that are safer and more sustainable, as well as more efficient and sustainable nano-manufacturing techniques [17]. At the same time, nanotechnology is critical for green innovation and growth, and is considered as a means of producing more sustainable non-nano materials and products, as well as assisting in the resolution of economic, environmental, and societal concerns [17]. The use of green

Table 1

Different kinds of new sustainable material which can be used for developing COVID-19 diagnostic system.

kinds	strength	Weakness
Paper	Naturally derived, simple to produce, easy available	inference from environmental condition, shelf-life
Cellulose	environmental friendly, easy to modify/combine with other material	inference from environmental condition
Graphene	adaptable in several designed molecule, nanomaterial characteristics	difficult to produce, required nanotechnology facilities

synthesized nanomaterials in optical biosensor devices may lead to more sustainable and environmentally acceptable solutions to the COVID-19 dilemma [15]. Using green synthesized materials in optical biosensor devices could lead to more sustainable and environmentally friendly solutions to the dilemma [15,18].

Here, the authors will briefly summarize on some interesting new green biotechnology of COVID-19 detection biosensor.

1. Paper-Based Biosensors for COVID-19 detection

Paper-Based Biosensors for COVID-19 is an example of applied sustainable materials in COVID-19 detection biosensor [19]. Microfluidic detectors made of paper are durable, cost-effective, and easy to use. They can be used to identify a wide range of viruses. There are numerous advantages to adopting paper-based devices, including the fact that this material is freely available all over the world and that its characteristics allow for straightforward liquid conveyance using passive flow [19]. In addition, several types of paper are compatible with printing and other patterning processes, extending their usefulness [19].

1.1 Paper-Based Biosensors for Viral Ribonucleic acid (RNA) Sensing

Since the emerging of COVID-19, lateral flow assays (LFA)s have been developed as available method for producing portable, low-cost diagnostics that do not require qualified personnel or specialized laboratory equipment. This follows the considerable development of LFAs in a variety of applications previously. LFA test strips made of nitrocellulose have been used to detect viral RNA in the case of SARS-CoV-2, after early proof of this technology in the creation of highly selective biochemical sensing techniques. In particular, novel biosensing technologies based on genetic material amplification and gene editing techniques have emerged in response to pandemic diagnostic needs, garnering widespread acceptance in both research and clinical contexts.

Regarding transduction techniques for paper-based biosensors for viral RNA sensing, it might be fluorescence, colorimetric, colorimetric/fluorescence or electrochemical. There are many applied schemes such as loop-mediated isothermal amplification (LAMP) pre-amplification + CRISPR cas12a + biotin-labeled ssDNA (single strand deoxy-ribonucleic acid) reporter, reverse transcription-recombinase polymerase amplification (RT-RPA) + clustered regularly interspaced short palindromic repeats (CRISPR) cas12a + biotin-labeled ssDNA reporter and RT-RPA + CRISPR cas13 + biotin-fluorescein RNA reporter [[19–21] [22]]. The well-known example of the biosensor in this kind is an antisense oligonucleotides directed electrochemical biosensor chip developed by Alafeef et al. [23] and a paper-based immunoassay based on 96-well wax-printed paper plate combined with magnetic beads for detection of virus in saliva developed by Fabiani et al. [24].

1.2 Paper-Based Biosensors for Viral Antigen Sensing

The detection of viral antigens specific to SARS-CoV-2, such as the N phosphoprotein and S glycoprotein, is an alternate method for SARS-CoV-2 identification. These viral structures aid in the early detection and diagnosis of circulating viruses in the body. This kind of test is already available as a self-test diagnostic test kit for general people to use during the pandemic (Fig. 1). Biosensors that target the S protein in relevant body fluids allow for the direct detection of complete virus particles and, in the case of protein N, the diagnosis of infection prior to the onset of symptoms and the organism's immune response [[19–21] [22]].

1.3 Paper-Based Diagnostics for SARS-CoV-2 Immunogenic Response Detection

When SARS-CoV-2 interacts with the human organism, an immunogenic response to viral antigens develops, which changes throughout the

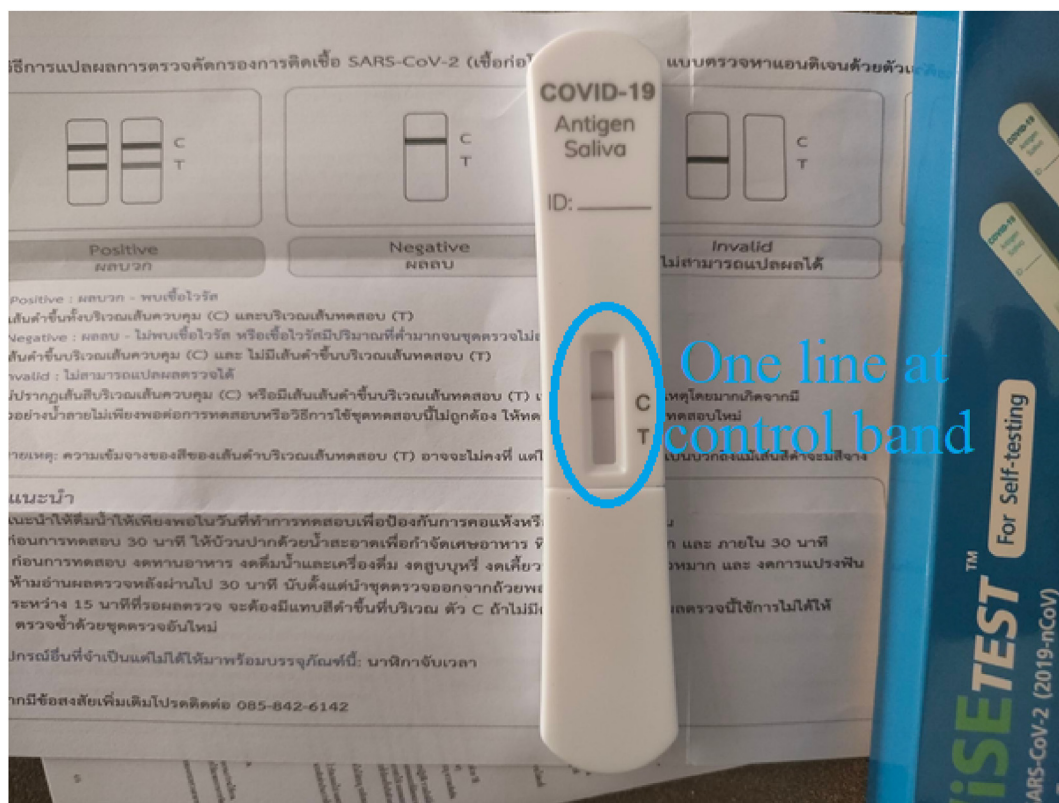


Fig. 1. Example of POC LFA sensor for antigen detection.

*The picture is an example of a negative COVID-19 case based on a locally available inexpensive antigen test sensor in an Asian country. The test is a self-performing test by a screenee based on available attached instruction in the figure.

stages of viral infection, from asymptomatic through symptom development and convalescence. Antibodies specific for SARS-CoV-2, primarily immunoglobulin (Ig)s including IgG, IgM, and IgA, are identified and quantified as part of the immunological response monitoring against COVID-19. Because it may serve as a diagnostic tool for current and past infections, as well as aiding in better controlling population immunity, serological detection of antibodies has been an important route in the control and study of this pandemic, especially now that vaccination is underway in multiple countries [[19–21] [22]].

LFA test strips appear to be a viable choice for immunological response monitoring since they combine the principles of thin-layer chromatography and immune recognition reactions to provide a rapid diagnosis with a low-cost visual transduction technique in times of need. Some research groups have looked into using this technique to detect IgG and IgM antibodies against SARS-CoV-2 using standard approaches like gold nanoparticle conjugation with specific SARS-CoV-2 antigens, as well as new approaches that use alternative reporter particles and different optical transduction mechanisms like SERS or fluorescence [[19–21] [22]]. At present, there is already a label-free paper-based electrochemical platform that targets SARS-CoV-2 antibodies without the need for a specific antibody [[19–21] [22]].

The benefits and cons of each type of paper-based biosensor are different (Table 2). It goes without saying that the development of new paper-based biosensor platforms with improved performance will aid in the containment of the COVID-19 outbreak by allowing for early detection at the point of care [[19–21] [22]].

2. Cellulose-Based Biosensors for COVID-19 detection

Cellulose has drawn a lot of attention, especially in medical applications such enhanced biosensing devices. Biosensors could benefit from cellulose's improved biocompatibility, biodegradability, and non-toxicity, which could be beneficial. As a result, they're important in environmental monitoring and medical diagnostics. Cellulose may usually be activated before enzyme immobilization, which could improve the biological element incorporation process or boost sensor efficiency [25,26]. One of the most frequent cellulose activation strategies is to use a cross-linking agent. Consecutive treatments with sodium periodate solution, ethylenediamine solution, and glutaraldehyde can activate cellulose. As a result, several enzymes can be immobilized on activated cellulose [25,28].

Cellulose and its derivatives have shown to be flexible materials with a good platform for immobilizing bioactive compounds in biosensors due to their unique chemical structure [27]. These cellulose-based biosensors have a number of appealing characteristics, including accuracy, sensitivity, ease, low cost, and quick response [27]. It has the advantages of being low-cost and simple to use. Nano-cellulose has a wide aspect ratio, good dispersing ability, and high absorption capacity, among other characteristics [27]. Optical and electrochemical cellulosic biosensors demonstrate two major kinds of quantifiable signal creation in the recognition/detection methods of cellulose-based biosensors [28]. Cellulose-based optical biosensors are of particular interest for label-free and label-driven (fluorescent and colorimetric) biosensors due to their simplicity, high sensitivity, and low cost. Several forms of cellulose substrates have been used in biosensors, including cellulose derivatives,

Table 2

Strength and weakness of different kinds of sustainable material -based biosensor.

kinds	strength	weakness
RNA sensing	Highly specific, early diagnosis	Cannot detect past infection more expensive
Antigen sensing	Specific, inexpensive	Window period of detection, cross antigen interference
Antibody sensing	Can detect past infection, inexpensive	Cannot detect early infection, Might require more than one test, cross antibody interference

nanocellulose, bacterial cellulose, paper, gauzes, and hydrogels [28]. For example, cellulose paper-based biosensors are low-cost and simple to use, but nano-cellulose biosensors are known for their good dispersion, high absorbance capacity, and huge surface area [28].

Cellulose-based biosensors can be particularly relevant in pandemic times, for the renewability, the possibility of mass production with sustainable methodologies, and safe environmental disposal [19]. Nevertheless, there are still limited reports on using cellulose-based biosensors for COVID-19 detection.

2.1 Cellulose-Based Biosensors for Viral Ribonucleic acid (RNA) Sensing

Similar to paper material, the cellulose based LFA for diagnosis of COVID-19 is available. Basically, nitrocellulose membrane can be used to add value to LFA-based diagnostic tools, which has a lot of potential for detecting COVID-19 in various environments [29]. A good example of the sensing system for RNA sensing is the recent sensing system developed by Tang et al. [29]. By integrating two sugar barriers into LFAs, one between the conjugation pad and the test line, and the other between the test line and the control line [29], LFA sensitivity was improved. The COVID-19 ORF1ab nucleic acid was employed as a model target on the HF120 membrane [29].

2.2 Cellulose -Based Biosensors for Viral Antigen Sensing

With the arrival of the post-COVID-19 era and the aging population, innovative biomaterials and bioelectronic devices are gaining in popularity [30]. Cellulose, one of the most prevalent natural polymers on the planet, has a number of advantages, including biocompatibility, processability, carbon neutrality, and mechanical designability [30]. Cellulose has a strong application promise in generating bio-functional materials due to its progressive progression of multi-scale design from macro to micro, followed by new cognitions [30].

An example of new cellulose – based sensing system for antigen sensing is the new biosensor for antigen detection using scFv-Fc fusion proteins developed by Kim et al. [31]. Kim et al. developed diagnostic antibody pairs for use on an LFIA platform based on cellulose nanobeads [30]. Because scFv-Fc antibodies bind to the SARS-CoV-2 NP antigen selectively and with great affinity, they can aid in the diagnosis of SARS-CoV-2 infection [31].

2.3 Cellulose-Based Diagnostics for SARS-CoV-2 Immunogenic Response Detection

Determination of Ig is an important diagnostic approach for diagnosis of SARS-CoV-2 infection. An example of new cellulose – based sensing system for Ig detection is a new LFA developed by Elter et al. [32]. In the study by Elter et al., development of cellulose paper-based LFA was developed using a carbohydrate-binding module-fused approach [32].

3. Graphene-Based Biosensors for COVID-19 detection

With its excellent physical and chemical properties, graphene, which is made up of single-layered graphite, has piqued the interest of scientists in a variety of fields, including electronics, medicine, and chemicals [33]. Its uses in green energy have been actively researched during the last few decades. The addition of biomacromolecules to graphene, such as DNA, protein, peptide, and others, expands graphene's potential applications in a variety of sectors [34]. The bound biomacromolecules might improve the biocompatibility and bio-recognition ability of graphene-based nanocomposites, significantly improving their biosensing selectivity and sensitivity [34]. The biofunctionalization of graphene with specially designed peptides, as well as the synthesis methodologies for graphene-peptide nanocomposites (monomer, nanofibrils, and nanotubes) are currently main topics in biosensor research [34]. In

comparison to other most effective materials, graphene is impermeable to gas and liquids, has superior thermal conductivity, and has a larger current density [35]. All of graphene's outstanding qualities have opened up new paths for its usage in nano-devices and nano-systems [35]. Several production approaches are also described, ranging from mechanical exfoliation of high-quality graphene to direct growth on silicon carbide or metal substrates, as well as chemical routes utilizing graphene oxide and a newly designed molecular approach [35]. The creation of graphene-peptide nanocomposite-based biosensor architectures for electrochemical, fluorescent, electronic, and spectroscopic biosensing are currently reported [36].

For application in laboratory medicine, the graphene – based biosensor is proven useful for diagnostic virology application [36]. Photoluminescence and colorimetric sensors, as well as surface plasmon resonance biosensors, are examples of graphene-based sensors for viral detection. For graphene-based sensing systems, several ways of electrochemical detection of viruses based on, for example, DNA hybridization or antigen-antibody interactions are possible, similar to the idea previously outlined for paper-based material [36]. Graphene-Based Biosensors for COVID-19 detection is an interesting innovation [37]. There are many ongoing researches on applying graphene for developing new biosensor for COVID-19 detection [37]. The new graphene - based field-effect transistor-based biosensor and gold nanoparticle (AuNP)-decorated graphene field-effect transistor (G-FET) sensor are good examples [38–40].

3.1 Graphene-Based Biosensors for Viral Ribonucleic acid (RNA) Sensing

Basically, nano-biosensors are capable of providing faster, more sensitive, less expensive, and high-throughput findings than traditional PCR and LFAs [41]. We can be far better prepared for future infectious disease outbreak control by developing novel technologies for sensitive, selective, quick, and robust viral detection, as well as more efficient ways for scaling manufacture of microfluidic devices. Graphene nanomaterials are current focuses for development of COVID-19 sensing system [42].

A good example of the sensing system for detection of virus is the recent report by Lit et al. [40]. In that study, a new graphene - based sensor for detection of SARS-CoV-2 RNA in human throat swab specimens was developed [40]. Li et al. established a fast and unamplified nanosensing platform [40]. A graphene field-effect transistor sensor with gold nanoparticles (AuNP) was made, and then a corresponding phosphorodiamidate morpholino oligos probe was mounted on the AuNP surface. The new biosensor not only had a low limit of detection in throat swab and serum, but it also had a quick response time in COVID-19 patient samples, taking only 2 min [40].

3.2 Graphene -Based Biosensors for Viral Antigen Sensing

An alternative way for identifying SARS-CoV-2 is to look for viral antigens specific to the virus, such as the N phosphoprotein and S glycoprotein. The early detection and diagnosis of circulating viruses in the body is aided by these viral structures. An example of new graphene – based sensing system for antigen sensing is reported by Jia et al. [43]. The system is based detection of the SARS-CoV-2 nucleocapsid protein by combining DNA/RNA oligomers as aptamers and a graphene oxide coated optical microfiber as a sensor system [43]. This system can rapidly detect the virus within 3 min [43]. Another example is a screen-printed graphene/carbon electrodes on paper substrates as impedance sensors developed by Ehsan et al. [44]. This new sensor detect of the SARS-CoV-2 spike protein utilizing the IgG *anti*-SARS-CoV-2 spike antibody [44].

3.3 Graphene-Based Diagnostics for SARS-CoV-2 Immunogenic Response Detection

Determination of Ig is a useful approach for COVID-19 diagnosis. An example of new graphene – based sensing system for Ig detection is a

highly sensitive graphene-based multiple-layer (BK7/Au/PtSe2/Graphene) coated surface plasmon resonance biosensor [45]. The system can help detect Ig using the virus spike receptor-binding domain as ligand and the virus anti-spike protein (IgM, IgG) as analyte [45].

3.4 Graphene-Based Diagnostics for SARS-CoV-2 Biomarker Detection

Apart from direct viral detection, determination of antigen and detection of antibody, graphene – based diagnostics for SARS-CoV-2 biomarker detection is one of the newest developments in biosensor science. At present, the graphene – based technology is already developed for detection of SARS-CoV-2 in the exhale breath sample. The detection of SARS-CoV-2 biomarkers in exhaled breath offers a quick and noninvasive technique to track the spread of COVID-19 [46]. Heptanal was discovered to be a critical biomarker that was considerably higher in SARS-CoV-2 patients' breath. Using density functional theory, the adsorption characteristics of heptanal on virgin and transition metal doped graphene can be investigated and used as a biomarker for COVID-19 diagnosis [46].

There are many sustainable materials for COVID-19 biosensor. A simple question is “Which material is more suitable for COVID-18 sensor?” Each kind of material has its specific strength and weakness. The selection of the materials should be based on the available data on the basic properties of the material (Table 1). Also, in the resource limited setting, the cost of the material also plays an important role. Finally, during the pandemic situation, there might be an urgent need of the diagnostic test. The simple and classic material might be easier to use for development of the sensing system. The advance material, such as new nanomaterial might have role, but it might require more time to get a success in the development of the new sensor. Therefore, it is no doubt that the classical paper based LFA is the currently most widely use sustainable material-based biosensor in clinical practice during the present pandemic.

A similar question might be raised regarding COVID-19 biosensor. A simple question is “Which sensor is more suitable for COVID-18 detection?” Similarly, each kind of sensor has its specific strength and weakness. The selection of the sensor should also be based on the available data on the basic properties of the sensor as well as the aim of diagnostic application. The performance metrics of the sensors should be considered. Key information includes limit of detection (LOD), sensing range, response time, and sensing conditions. LODs of the different biosensors are different (Table 3). The evaluation of the analytical performance is necessary for selection of the appropriate test. For evaluation, an LOD of 5.0×10^2 pfu/ml or 1.0×10^6 genome copies/ml in culture media is defined as acceptable by the World Health Organization [47]. The sensing range of the sensor also depends on the type of clinical samples and sensing condition. A fresh sample should be immediately tested as

Table 3
Performance matrices of different kinds of sustainable material -based biosensor.

Performance ^a	RNA sensing	Antigen sensing	Antibody sensing
LOD (pfu/ml)	$\leq 5.0 \times 10^2$	$\leq 5.0 \times 10^2$	$\leq 5.0 \times 10^2$
Clinical sensitivity (%)	100	85–95	85–90
Clinical specificity (%)	100	90–99	90–99
Response time (minute)	15–30	3–15	3–15
Sensing condition	Fresh collected sample, room temperature, no transportation media	Fresh collected sample, room temperature, no transportation media	Fresh collected sample, room temperature, no transportation media

^a according to Ref. [47] and available data from Thai Department of Medical Sciences Ministry of Public Health (<https://www3.dmhc.moph.go.th/>).

soon as possible after specimen collection. The transport media can interfere the analytical performance of the sensor [47]. Prolonged storage in freezing condition might help lower the reduction of analytical sensitivity but it is not recommended. These critical points in pre-analytical quality management should be recognized and it can help reduced aberrant laboratory results due to pre-analytical error (Fig. 2).

In the real clinical use, selection of the sensor should also be based on the aim of the diagnostic investigation. The screening and definitive diagnostic purpose might require different kinds of sensor. The screening should select a sensor with high sensitivity for case inclusion. However, it has to recognize on the possible false negative problem. Whereas a definitive diagnosis requires a sensor with high specificity, which might mean a possibility of false positive. Therefore, to select a sensor for a real clinical use, it is necessary to consider in context of diagnosis. For example, if it required a gold standard for definitive diagnosis, the RNA sensing system should be selected. On the other hand, in case of a mass screening such as epidemiological study, an immune response sensing system might be selected. Finally, in clinical use, the appropriate sensor at different period of infection is different. At a very early stage, a sensor that detect RNA might be more appropriate whereas the sensor that detect antibody is more appropriate for detection of past infection (Fig. 3).

4. Fabrication of sustainable material -based COVID-19 detection biosensor

During the COVID-19 pandemic, mass infection testing is essential, as previously stated. Normally, a fast POC test is necessary. The field of

microfluidics offers an alternative to time-consuming bench assays. Microfluidic devices capable of manipulating minute volumes of fluids and extracting information have emerged in just a few decades with the use of microelectronics and micro-electromechanical systems technology. Fabrication is the process of creating a part or product from scratch using raw or semi-finished materials. This can range from simple composite constructions to complicated composite structures. Basically, there are several fabrication techniques for creating a biosensor. Various sorts of biosensor fabrication processes recently published in the literature for COVID-19 diagnostics. Emerging telemedicine technologies have been developed to solve the inadequacies in COVID-19 diagnoses, monitoring, and management, due to the rise of mass-fabricated electronics for wearable and portable sensors [48]. Of several techniques, printing and cutting, molding and photolithography are commonly frequently used techniques for the fabrication of microfluidic detectors [49].

4.1. Printing and cutting

This technique is usually applied to the paper-based biosensor. The goal of many flow control systems is to slow the fluid down. This, however, may result in longer test durations and sample loss due to evaporation. Prininting and cutting can be applied in the fabrication process. Three-dimensional (3D) printing enables the production of anatomically matched specific devices [50]. Non-contact and contact printing are the two sorts of standard printing methods. The printed patterns are defined by moving the stage or nozzle in a non-contact printing method, which uses an ink solution delivered through nozzles. Contact printing, on the other hand, necessitates the use of a mask or patterned roll that

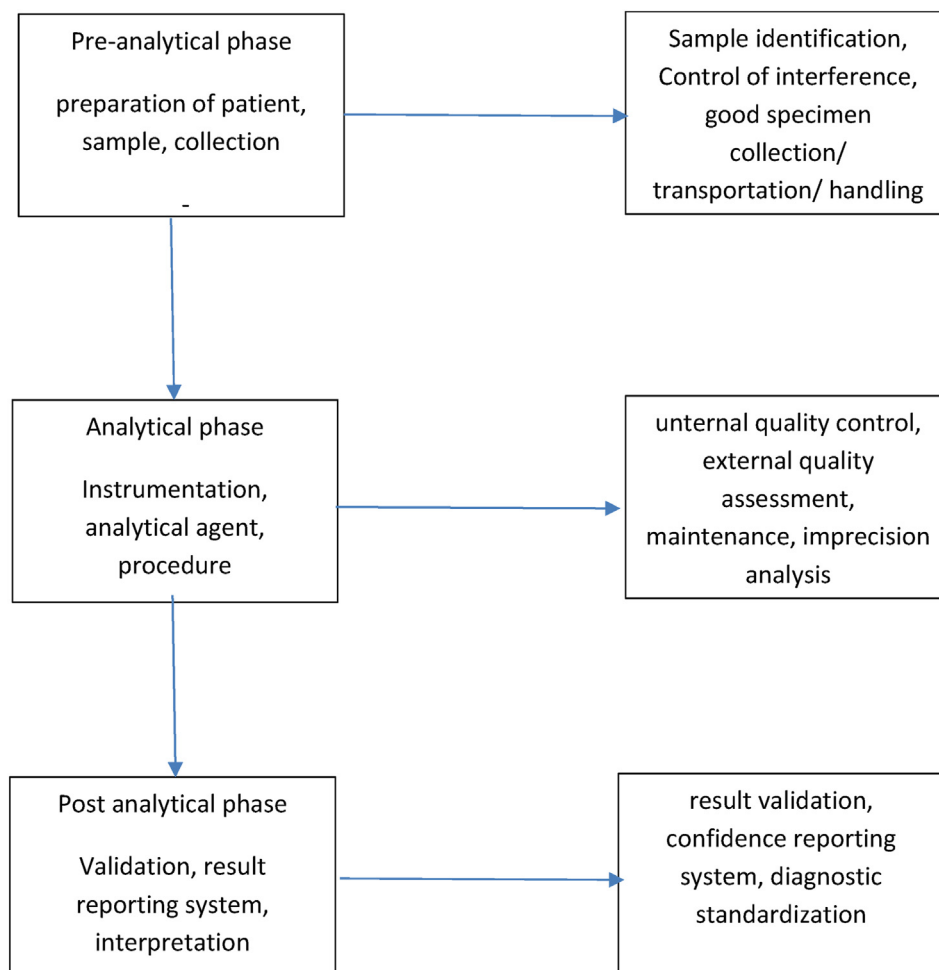


Fig. 2. Quality control according to laboratory medicine principle.

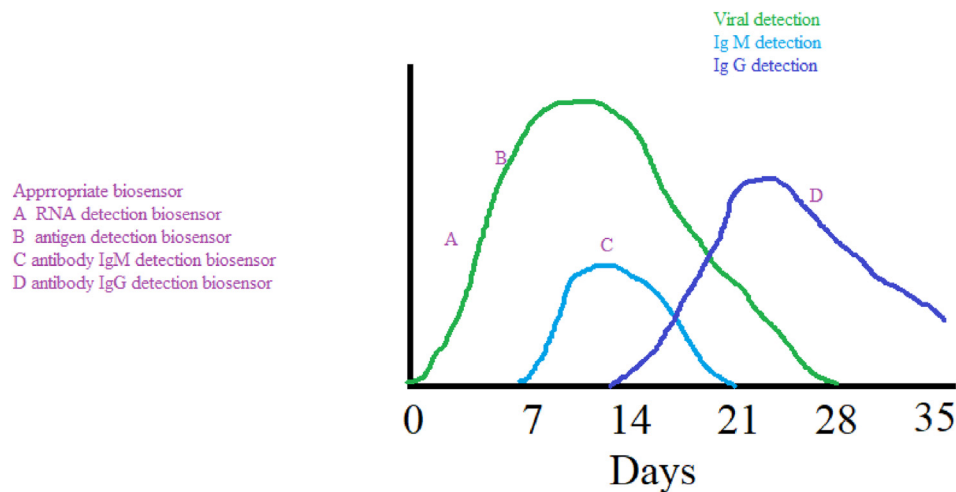


Fig. 3. Appropriate biosensor at different period of COVID-19 illness.

makes actual contact with the substrate to print [51,52]. 3D printing is a type of additive manufacturing technology in which successive layers of material are used to construct a three-dimensional object [52]. Other additive manufacturing technologies are slower, more expensive, and more difficult to use than 3D printers. They allow designers to print components and assemblies composed of a variety of materials with varying mechanical and physical qualities in a single production process [52].

Laser cutting is a possibility. Lasers may write on a workpiece directly or through a mask, allowing them to be utilized for machining of lower volume microfluidic devices, such as generating holes, channels, and complicated 3D geometries, as well as connecting and changing surface properties [52,53]. To speed up wicking speeds in paper-based microfluidic systems, a laser creates engraved grooves on the paper. The fastest wicking channels were produced by merely cutting a slit into the paper. The incision functioned as a macro capillary, allowing fluid to bypass the paper and accelerate the process [51]. 3D printing and cutting is currently widely used in production of paper based LFAs for COVID-19 diagnosis [53]. A good example of biosensor developed by printing and cutting fabrication for COVID-19 detection is the graphite – based biosensor developed by Stefano et al. [54].

4.2. Molding

Fabrication of microstructures via machining techniques can be costly due to equipment capital expenditures, but it can also be time-consuming. If micro- or nanoscale processes can be replicated, manufacturing costs can be drastically lowered [53]. A variety of micro-replication processes may be employed to fabricate a wide range of devices, most of which are built of polymers. For the manufacture of microfluidic devices, compression molding and injection molding are commonly used [53,55]. For COVID-19 biosensor, molding is limited used.

4.3. Photolithography

Photolithography is a well-known technique for micro- and nano-fabrication. A light source (e.g. UV radiation), a mask, and a photoresist-coated substrate are the basic components of this method [55]. A good example of new COVID-19 biosensor development based on this fabrication technique is the silver and gold metal nanoparticle - based sensor developed by Prabhakar et al. [56]. There is no report on using photolithography for developing of a sustainable material-based COVID-19 biosensor.

5. Advantages and disadvantages of sustainable materials for COVID-19 detection biosensor

Sustainable materials are currently accepted as useful materials in modern life. The sustainability is already extended to the novel production of new nanomaterials. Green chemistry concepts can be used to make nanomaterials that are safer and more sustainable, as well as more efficient and sustainable nano-manufacturing techniques [17]. At the same time, nanotechnology is critical for green innovation and growth, and is considered as a means of producing more sustainable non-nano materials and products, as well as assisting in the resolution of economic, environmental, and societal concerns. Non-renewable resources are not depleted by a sustainable substance. When used, it has no negative influence on the environment [17]. Simply put, sustainable materials are materials that can be produced in adequate numbers without depleting non-renewable resources or disrupting the environment's and key natural resource systems' established steady-state balance [15,16]. The biosensors are used for early detection and are important in preventing illness progression throughout the body. Because paper and paper-like materials are inexpensive, plentiful, and biodegradable, they have recently become popular for POC testing devices (e.g. nitrocellulose membrane) [16]. Microfluidic paper-based analytical devices have a lot of potential because they are inexpensive, easy to use, quick, precise, and long-lasting in a range of conditions [16].

Biosensing with sustainable materials is friendly to the environment and can help reduce waste. When it is applied in clinical biosensing, it is extremely useful since there are numerous diagnostic tests in each day. For the current COVID-19 pandemic, a rapid shooting of laboratory tests occurs and if there is no implementation of the environmentally friendly testing, the problem of clinical waste can occur. Infectious waste, in addition to the problem of ordinary sanitation, will become a major challenge that pollutes the environment during the COVID-19 pandemic [57]. In the case of COVID-19 pandemic, the waste might be highly infectious and contagious, therefore, the reduction of the waste as much as possible is the important principle [57].

It is no doubt that the sustainable materials have several advantages in biosensing. However, the demerits/limitations of these methods are little mentioned. The sustainable material -based biosensor can provide fast diagnostic result, which is not different from general biosensor. However, the degradable property should be carefully considered. A good keeping of the sustainable material -based biosensor is needed. Some extreme environment, such as too hot or too humid conditions might result in impaired diagnostic properties of the assays. The shelf-life of the sustainable material -based biosensor might be short and if there is no good plan for stock, the problem of expiration might occur and it can

result in loss of resources. The degradation of the material is a good property that is friendly to the environment in one hand, but it might mean the shortening of the shelf-life of the sensor. How to find a new sustainable material that has can be used for a long period of time is still a challenge. Also, the system to monitor the quality of the sensor at different time after production to certify its remained good analytic performance is still another main challenge. Indeed, the quality control and rechecking of the quality before use is a general rule in laboratory medicine for using POC. At present, sustainable material -based biosensor is a new thing and there is still no standard guideline from international clinical diagnostic society on standardization and quality management, hence, it might be difficult for practitioner to manage it. Nevertheless, the basic standard principle for total quality management in clinical medicine might be applied. The control of quality from pre-analytical, analytical and post-analytical phase must be applied [58]. Finally, it is necessary to have a validation of the clinical diagnostic properties of the sustainable material -based biosensor before using. Most available reports are on the analytical performance based on chemistry/material science evaluation. Clinical evaluation in real clinical settings is required for final conclusion on the diagnostic property of any new sustainable material -based biosensor. Based on authors' point of view, the advantage of new sustainable material -based biosensor is over disadvantage. Nevertheless, it is necessary to have a good clinical diagnostic practice in using of the new sustainable material -based biosensor in order to achieve the best clinical diagnostic utility. At present, different testing methods can be based on the sensing of targets, which include RNA, spike proteins and antibodies as earlier mentioned [59]. New nanotechnology might be applied to improve the analytical performance [60]. Electrochemical sensing has various advantages, including high selectivity, relatively low-cost apparatus and sensors, user-friendly operation, and quick analysis, all of which are ideal for downsizing to POC analyzers [61,62]. The new POC approach has a number of advantages that allow it to overcome the limitations of transporting to the nearest pathology laboratory, allowing it to be used in resource-constrained settings [62]. Due to biocompatibility, nanomaterials were employed to alter the electrode, preventing electrode fouling and improving detection limit, selectivity, and sensitivity [61]. However, limited data from real clinical evaluation of the clinical diagnostic interference are available. The importance of basic clinical laboratory quality management should be highlighted. A practitioner has to follow the standard principles of quality management in laboratory medicine. The evaluation of the test before use is needed and there should be continuous quality surveillance of the assay. A study on the interference of the test as well as error analysis is required and the derived data can be useful for further continuous improvement for finding a new generation of sustainable material -based biosensor to serve the rapid change of the COVID-19 pandemic situation. Finally, the main challenges unresolved for any diagnostic tools for COVID-19 including to sustainable material - based biosensor is the rapid change of the pathogen. Several new variants of SARS-Co-V2 occur within a short period. The development of the new biosensor might firstly be based on the old pathogen which might not be able to correspond to the newly change variants. The diagnosis of COVID-19 during the emergence of new variant of pathogen is usually problematic and it might be associated with an influx of increasing number of required tests in an extremely short period [63]. Therefore, a continuous improvement of the sensor is required. Searching for the new generation biosensor to correspond to the new emerging pathogen variant is required.

6. Some advanced sustainable material - based biosensor for COVID-19 diagnosis

In addition to the general biosensor, there are also attempts to develop some advanced sustainable material - based biosensor for COVID-19 diagnosis. Some different advanced systems are used for used for construction of new sensing of COVID-19. This is the trend for future

research and developing of clinical biosensor for COVID-19 diagnosis, Examples of important advanced sustainable material - based biosensor for COVID-19 diagnosis will be further discussed.

6.1. Field-effect transistor-based biosensor

A biosensor field-effect is a field-effect transistor that is gated by changes in the surface potential generated by molecule attachment. This technology has already been used in development of some new biosensor for COVID-19 diagnosis. The performance of biosensors based on field-effect-transistors improves dramatically when nanotechnology is used, particularly when nanomaterials such as graphene, metal nanoparticles, single and multi-walled carbon nanotubes, nanorods, and nanowires are used. Furthermore, their commercial availability and large-scale, high-quality production make them one of the most popular sensing and screening platforms [64]. For example, Seo et al. developed a new field-effect transistor-based biosensing device for detecting SARS-CoV-2 in clinical samples [39]. The system is based on a specific antibody against SARS-CoV-2 spike protein coated graphene sheets of the field-effect transistors [39]. Seo et al. found that the new sensor had a very good analytical performance with LOD equal to 2.42×10^2 copies/mL [39]. At present, there are some new field-effect transistor-based biosensor that can help simple clinical diagnosis based on saliva samples [65,66].

6.2. Wearable biosensor

Telemedicine or mobile health is well-positioned during this period to limit disease spread and overburdening of the healthcare system through at-home COVID-19 screening, diagnosis, and monitoring [48]. With the introduction of mass-fabricated electronics for wearable and portable sensors, new telemedicine technologies have been created to address limitations in COVID-19 diagnosis [48]. When an asymptomatic individual with COVID-19 exposure is isolated, temperature and symptom observation are required [67]. As a result of its intermittent nature and significant reliance on self-discipline, surveillance has limited effectiveness [67]. Wearable biosensors in a range of form factors can now be used to continually monitor physiological indicators thanks to advancements in biosensor technology [57].

7. Conclusion

The current global issue is COVID-19. The pandemic's billions of infected cases necessitate quick action to keep the outbreak under control. The importance of early discovery and treatment in containing the outbreak cannot be overstated. The development of new COVID-19 biosensors that are rapid, reliable, and sensitive has sparked a lot of interest. Although there are some reports on the new biosensors for COVID-19 diagnosis, there are limited reports on the sustainable materials - based biosensor. Additionally, less data on a systematic review of the sustainable materials - based biosensor is available. The present article provides an overview from a systematic review for this specific topic. Most previous publications are focused only on the material science aspects of the biosensor, such as fabrication technique and properties. The present study adds the concern in the real clinical use of the sustainable materials - based biosensor, which is the exact usefulness of the sensing system. The novelty from this article also includes the point of view on selection of the materials and sensor based on clinical concern for the current COVID-19 pandemic situation. The biosensors would be a one-step method of identifying or sensing. Biosensors have already demonstrated their ability to provide cost-effective and accessible diagnostics, with applicability in situations where traditional laboratory techniques are not easily available. Paper- and cellulose-based biosensors are particularly useful in pandemic situations because of their recyclability, ability to mass-produce using sustainable methods, and safe disposal. The contemporary concept of sustainable materials is in line with the current

trend of green and environmentally friendly technology. The application of green synthesized nanomaterials in optical biosensor devices could lead to more long-term and environmentally friendly COVID-19 solutions.

Declaration of competing interest

None.

List of abbreviations

ACE-2	angiotensin-converting enzyme 2
AuNP	gold nanoparticles
CRISPR	clustered regularly interspaced short palindromic repeats
COVID-19	coronavirus disease 2019
CT	computerized tomography
Ig	immunoglobulin
LAMP	loop-mediated isothermal amplification
LFA	Lateral flow assay
LOD	limit of detection
POC	point-of-care
RNA	Ribonucleic acid
RT-PCR	reverse transcription polymerase chain reaction
RT-RPA	reverse transcription-recombinase polymerase amplification
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
ssDNA	single strand deoxy-ribonucleic acid
3D	three-dimensional

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