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Paper-Based Point-Of-Care Biosensor for Covid-19

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Abstract

Corona virus disease 2019 (COVID-19) outbreak has developed into a universal pandemic. The harmful effects of corona virus have provoked the advance of diagnostic tools to supervise the spread of disease. While conservative technologies have been mostly used to detect COVID-19, they are protracted, manual and are unavailable in distant settings. Point-of-care (POC) biosensors, including paper-based biosensors are characteristicallylow-priced and accessible, which presentincredibleprospective for speedy medical diagnosis. In view of the risinginsist for quick diagnosis of COVID-19, a mini review that summarizes the currentadvancement in developing POC biosensors for COVID-19 is exceedinglyattractive. In this article, the most modern advances in POC biosensors, including paper-based biosensors for the recognition of COVID-19 infection are reviewed.

INTRODUCTION

Paper-based biosensors have fascinated additional considerable interest for utilize in POC testing as compared to chip-based biosensors due to their biodegradability and cost-effectiveness, as well as functionalization, modification and ease-of-fabrication[1]. With this distinctiveness, they are competent to accomplish quick, onsite POC testing in inaccessible settings. [2] Lateral flow test strips have been extensively used for the recognition of COVID-19. [3]They are premeditated to notice IgG and IgM in patient serum, whole blood and plasma samples. Each test strip usually consists of (i) a sample pad to append patient samples, (ii) a conjugate pad containing COVID-19 antigen conjugated with gold nanoparticles and gold-rabbit IgG, (iii) a nitrocellulose membrane that consists of a control line encrusted with goat anti-rabbit IgG, an IgG test line coated with anti-human IgG, an IgM test line encrusted with anti-human IgM as well as (iv) an absorbent pad that absorbs waste. [4] In the existence of IgM and/or IgG in patient samples, the antibodies respond with gold-COVID-19 antigen to form a complex, which moves transversely the nitrocellulose membrane and interrelate with the anti-IgM and/or IgG at their individual test line. The gold-rabbit IgG in turn reacts with anti-rabbit IgG encrusted at the control line to generate a visible red color. A positive IgM and a negative IgG or positive at both lines designate a principal or acute infection, while a positive IgG with a negative IgM shows a resulting or later stage of infection. [5-7]

Apart from antibody testing, various lateral flow test strips with sample-to-answer capability have been used for nucleic acid testing which could potentially identify COVID-19 nucleic acids in respiratory samples. For example, a assembly has introduced a completely incorporated paper-based biosensor that involves three main steps of nucleic acid testing, producing colorimetric signal detected by lateral flow test strip. [8-9]Conversely, this incorporated biosensor requires a peripheral heat block for amplification. To abridge the platform for POC applications, a small and transportable heater has been developed in permutation with four-layered paper-based sample-to-answer biosensor. This biosensor consists of Fast Technology Analysis (FTA) card and glass fiber for nucleic acid extraction and LAMP, along with an incorporated lateral flow test strip for visual recognition. [10-11] Each functional film is alienated by hydrophobic polyvinyl chloride substrates that manage the fluid flow from one layer to another. To promote abridge the processes; a semi-automated, entirely disposable and incorporated paper-based biosensor has been developed (Tang et al., 2017c). This integrated biosensor consists of a paper-based valve and a sponge-based reservoir to extract nucleic acids from crude samples, a portable battery and a heater integrated into the platform for isothermal amplification (i.e., helicase dependent amplification, HDA) as well as a lateral flow test strip for colorimetric detection. The proposed biosensor allows on board reagent storage with the use of sponges and equipment-free isothermal amplification which significantly simplifies user steps. More recently, lateral flow test strip has been combined with paper folding technologies for sample preparation, LAMP and lateral flow detection. [12] The integrated test strip consists of buffer chambers that regulate fluid flow, acetate films which prevent sample evaporation, filter paper-based valves that prevent LAMP reagent from mixing with other reagents, and a lateral flow test strip. This incorporated knowledge is appropriate for use in inaccessible settings to check crude samples, contribution huge possible to quickly notice nucleic acids of COVID-19 (<50 min). [13-15]

Moreover, lateral flow test strips, numerous 3D paper-based micro fluidic biosensors have been developed to perceive proteins or nucleic acids at the POC. These biosensors typically notice targets based on fluorescence or colorimetric detection approaches. Metal ions have been used in 3D paper-based micro fluidic biosensors to respond with base from double stranded DNA to form a stable complex that demonstrate fluorescent signal leading UV irradiation. For instance, completely incorporated and foldable biosensors encapsulated with agarose have been developed for long-term reagent storage and multiplex fluorescence detection. [16]The

biosensor consists of a response zone and a recognition zone. Agarose that carries LAMP reagents and silver nitrate is deposited and stored in response and recognition zones for at least 45 days. The sample is added into reaction zones which are then bunged with an adhesive sealing coat to avoid sample vanishing prior to being positioned on a portable heater for amplification. [17] Subsequent the amplification process, the sealing film is detached and the recognition zone is folded and flooded into the response zone. UV light is used to imagine the response between amplicons and silver ions. The brown color intensity of the test zone augmented along with the increased concentration of amplicons. The biosensor is easy and consumer friendly, which is predictable to notice COVID-19 nucleic acids in patient samples. [18-20]

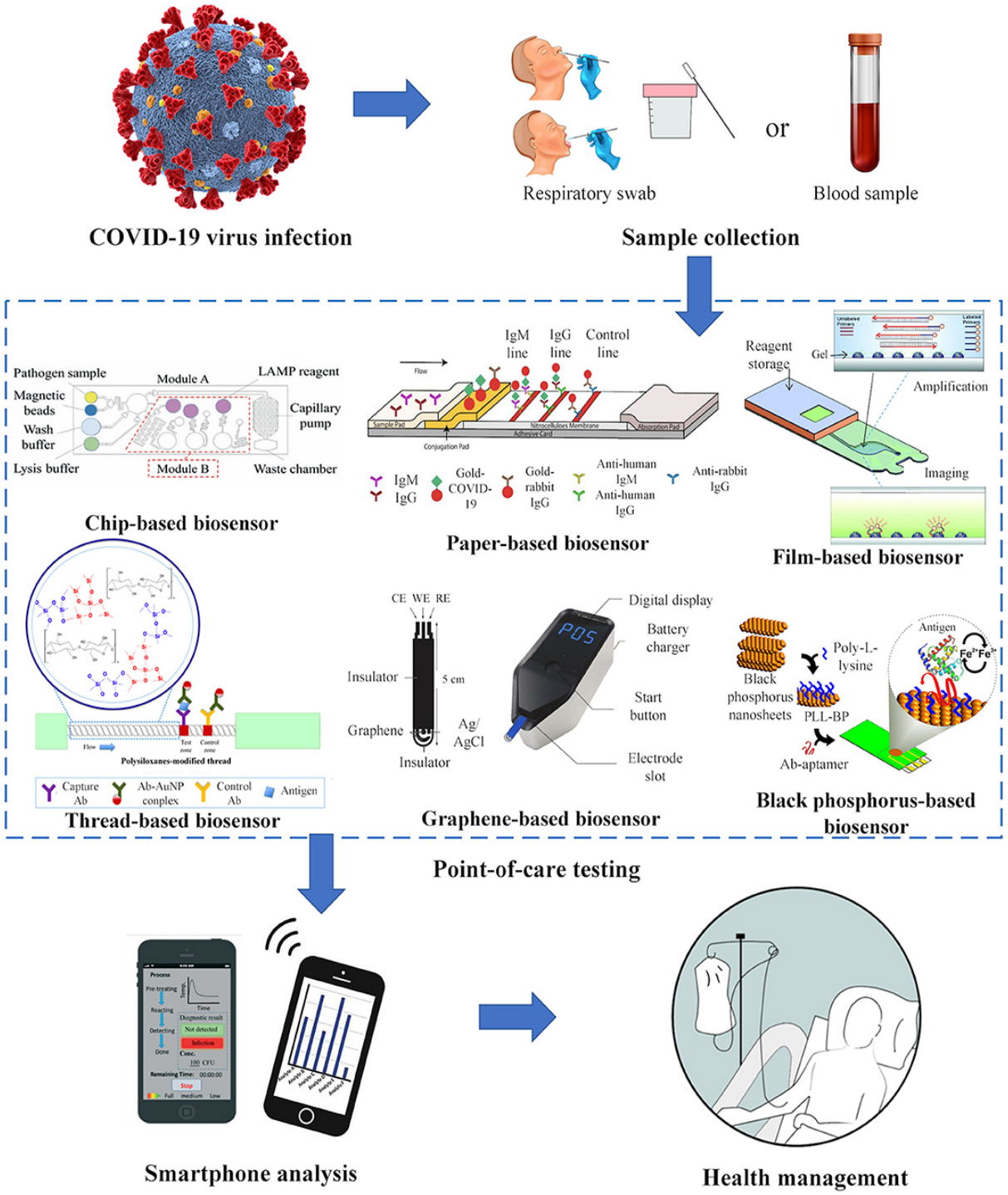

Figure-1: Point-of-care biosensor for Covid-19

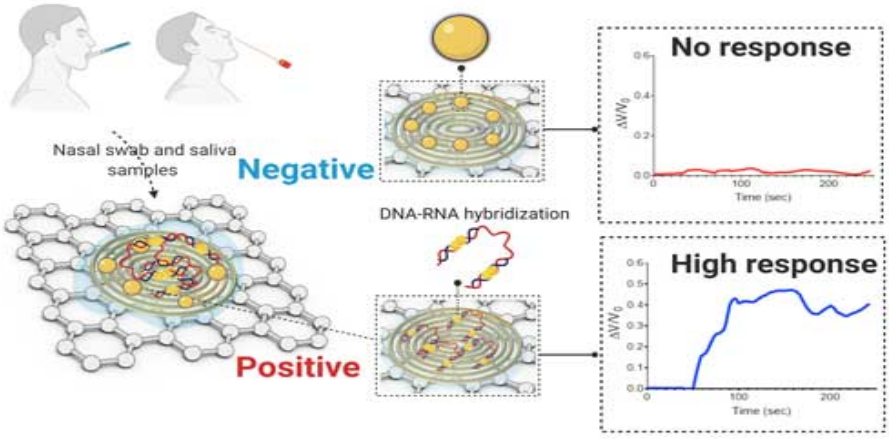

Figure-2: COVID-19 electrochemical sensing proposal

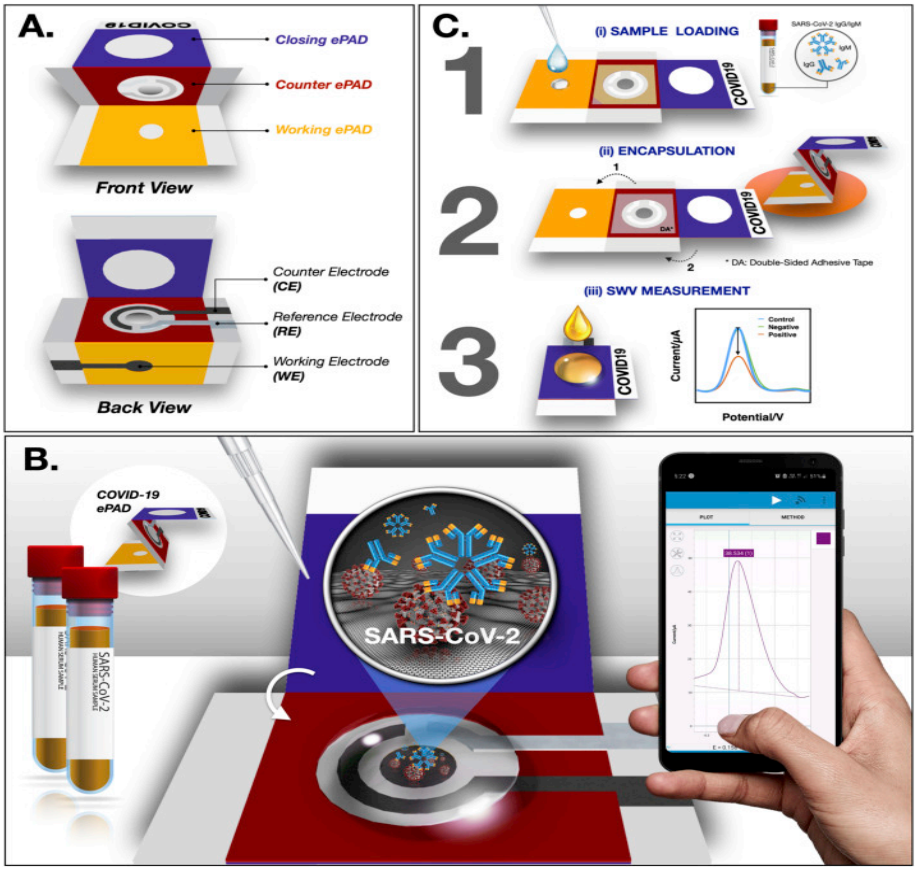

Figure-3: Schematic illustration

Newly, as a new substitute, fuchsin has been explored for the recognition of DNA amplicons based upon colorimetric detection approach using a 3D paper-based microfluidic biosensor. In the lack of DNA amplicons, adding of sodium sulfite molecule and fushsin produces fushsin leucosulfonic acid or leucofushsin which is neutral. [21]In the attendance of DNA amplicons, aldehyde groups of the DNA bind to sulfonate groups and the link between hydrogen sulfite and the central C atom is busted, producing the fuchsin with chromophoric structure, which appears to be purple. The anticipated biosensor is composed of a sample zone, a response zone and a recognition zone. [22]The recognition zone consists of paper strips with fuchsin stained lines. Momentarily, sample is injected into the sample zone which is conserved with an adhesive sealing coat to avoid sample vanishing. The response zone is folded to combine to the sample zone and the biosensor is twisted upside down to allow the flow of sample from sample zone to response zone. [23] The biosensor is excited on a hot plate at 65°C for 30 min for LAMP. After LAMP, the sealing layer is peeled off and the hydrochloric acid is injected into the response zone. Sodium sulfite is consequently added and the changes of fuchsin-stained line color are pragmatic. Contrasting the above-mentioned biosensors, this biosensor produces effortless colorimetric signals noticeable by the naked eyes devoid of requiring any

exterior readers, which shows hopeful for express diagnosis of COVID-19 infections at the POC. [24]

Antibody tests are appropriate to detect the delayed stage of infections while nucleic acid tests detect the existence of nucleic acids (viruses) at the premature stage of infection, viewing a superior sensitivity and specificity than antibody tests. Conversely, existing nucleic acid tests necessitate three key steps (i.e., nucleic acid extraction, amplification, and detection), concerning further convoluted processes than that of antibody tests. In fact, nearly all of the marketable POC biosensors for COVID-19 are paper-based biosensors or lateral flow test strips for antibody detection (IgG and IgM) that generate colorimetric signal. Whereas these antibody tests exhibit inferior specificity compared to nucleic acid tests, they have helped restriction the turnaround time for quick diagnosis, allowing fast resolution making. Prospect work is supposed to comprise specificity development or permutation with further tests such as rapid nucleic acid tests to authenticate the test result. [25-27]

The biosensors discussed in this review show enormous impending to be developed into a independent platform for the recognition of COVID-19 infections exterior the laboratory, chiefly in the inaccessible settings or developing areas. [28]

CONCLUSION

Prospect studies should advance progress the purpose of Smartphone and precise smartphone apps that facilitate on-site data analysis while allowing data storage to way patient health status. Furthermore, incorporating portable power sources such as batteries into biosensors would considerably precede their functionality in rural areas where power supply is restricted. In short, promising POC biosensors with the above-mentioned capabilities might speedily recognize the spread of COVID-19 and direct suitable health care, in concert a key function in supervision the outbreak.

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