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Review Article

Biosensors - An Insight into the Electrochemical and Optical Biosensors

Sri Nataraj Kalakonda[1], Rani Bammidi[1,*], Harika Edubilli[1], Sangeetha Medapati[1], Sahantha Lakshmi Deepthi Boyina[1], V V S Rajendra Prasad[2]

[1]Department of Pharmaceutical Analysis, Shri Vishnu College of Pharmacy, Bhimavaram, Andhra Pradesh, INDIA.
[2]Department of Pharmaceutical Analysis, Vishnu Institute of Pharmaceutical Education and Research, Narsapur, Telangana, INDIA.

ABSTRACT

The upgrading of useful biosensors having advantages in disease monitoring besides detection has been sped up by the demand for quick, cheap, portable, easy screening procedures. Bioanalytical devices such as Biosensors have a number of distinguishing benefits over conventional analytical techniques, including high accuracy and specificity, ease of handling, economic friendly, and the potential for downsizing and mass production. With an emphasis on electrochemical and optical sensors, this study examines current developments in the design, performance, and applications of biosensors. Due to its advantages of high sensitivity, specificity, and rapid analysis, electrochemical sensors have demonstrated a wide range of applications in biological detection whereas the optical biosensors covered in this article have enabled diagnosis of SARS-CoV-2, which highlighted the importance of creating swift and extremely sensitive diagnostic methods for quickly identifying infected patients using LSPR, SERS, FET, EC biosensors.

Keywords: Bioanalysis, Biosensors, Electrochemical, Optical, SARS-CoV-2, Localized Surface Plasmon Resonance, Surface Enhanced Raman Scattering, Electrochemical, Field Effect Transistor.

Correspondence:
Ms. Rani Bammidi
Department of Pharmaceutical Analysis, Shri Vishnu College of Pharmacy, Bhimavaram, Andhra Pradesh, INDIA.
Email: bammidirani1999@gmail.com

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INTRODUCTION

In the biomedical, environmental, and food quality control, agricultural, and pharmaceutical industries, enzyme-based biosensors have become an important tool for qualitative and quantitative measurement of a variety of target analytes. In the healthcare field, biosensors have advantages such as quick, extra-laboratory analysis and significantly lower sample costs. They provide considerable advantages over traditional analytical approaches, including, accuracy, quicker sample preparation, and ease of handling, since they can be useful in the disease detection.

An all-encompassing definition of a biosensor is "a self-contained analytical device that integrates a biological component with a physicochemical device for the detection of an analyte of biological importance". It contains a transducer that can turn this connection into a measurable signal and a biological recognition element that can specifically engage with a target molecule.

Chemical biosensors work by detecting the biological component that is unique to the analyte and steady when used and stored normally. Biosensors have utilized a wide range of recognition components, including receptors, nucleic acids, entire cells, and many enzymatic classes.

Typically, biosensors are categorized based on the transduction technique they employ. A huge number of chemical, physical, or biological interactions are transformed into an electrical signal by the transducer in biosensors. This has led to the development and characterization of optical, calorimetric, or acoustic biosensors; nonetheless, the electrochemical properties of transducers and analytes are what make biosensors so popular.

A small number of biosensors are currently on the market (such as sensors for diabetes monitoring), whereas the majority are still in the development phase. Traditional enzyme-based biosensing designs for *in vivo* detection have been covered in a number of excellent reviews. These designs include optical and electrochemical sensors.[1-4]

ELECTROCHEMICAL BIOSENSORS FOR BIOMEDICAL ANALYSIS

The electrochemical biosensor keeps track of the electrochemical signal that results from the interaction of the target molecules (analyte molecules) and the detecting probe. Different electrochemical techniques, such as potentiometry, amperometry, electrochemical impedance spectroscopy, and cyclic voltammetry, can be utilized with electrochemical biosensors depending on the target molecules and environment.[5-8]

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In particular, composites, conducting polymers, biopolymers, and nanomaterials have been used to create electrochemical biosensors.[9-15] An analyte, receptor, transducer, and recording system are components of electrochemical biosensors.[16] Acetylcholinesterase, for instance, can be a receptor that functions as a biorecognition element for an analyte. These enzymes are able to generate electrons with recognized signals.

Drug-DNA interactions, disease and biomarker identification are all common uses for DNA biosensors. Due to their potential and economic availability, DNA biosensors are also chosen for gene identification.[17-22]

For the detection of microbes, viruses, lipoproteins, bacteria, and food pathogens, immunosensor-based biosensors are chosen. When creating electrochemical sensors, it is important to keep in mind that they can either make simultaneous or multiplex measurements or have enhanced selectivity. Their shelf life is between six months and a year, which is short or limited. Other substances can interfere with some electrochemical sensors. Knowing the substances that might interfere with the suggested sensor is crucial. The most popular electrochemical biosensors will be discussed in this review.

Electrochemical DNA Biosensor

Drugs, particularly those with anticancer, antiviral, and antibacterial properties, primarily target the cellular DNA. Covalent and non-covalent agents can be used to categorize DNA-interacting substances in general. Covalent bonding results in cell death and is irreversible. The non-covalent binding can alter DNA conformation, is reversible, and may result in DNA strand breakage. In order to build DNA-targeted medications and to understand how drugs interact with DNA, studies on this topic are essential.[23-25]

Electrochemical DNA biosensors are a superb tool for the diagnosis of DNA thanks to modern technology and device downsizing. Usually, during electrochemical detection of DNA hybridization, a current at a fixed voltage is observed. In the realm of nucleic acid analysis, numerous efforts have been made to utilize the contemporary electrochemical methodologies. One of the best methods for finding cancer biomarkers early is to use DNA-based electrochemical biosensors.

DNA-based biosensors gather target DNA's information in order to generate an electrical signal for that particular analyte to be examined. Different sorts of immobilization strategies exist achieve rapid, precise steadiness depending on the transducer's qualities. The immobilization and hybridization processes are influenced by electrode surface modification using various nanoparticles. Due to its ability to identify little concentrations of oligonucleotides, single-base mismatches, DNA biosensors can quickly identify cancer biomarkers produced by malignant cells.

This section discusses particular DNA-based biosensor for functionally based identification of CYFRA 21-1 biomarker.

CYFRA 21-1 is regarded as a useful biomarker for the identification of NSCLC. As shown in Figures 2, (A- C) created a DNA-based biosensor for the detection of CYFRA21-1 using functionalized three-dimensional graphene and AgNPs (3D GF/AgNPs).

A probe DNA with the sequence 5′ - S H - G A A G G G A G G A A T G G T G T C A G G G G C G - 3′ was utilized to track the complementary DNA 5′-CGCCCCTGACACCATTCCTCC-CTTC. After PCR amplification, the isolated genomic DNA from a clinical sample was electrophoresed. Without any binding, lambda-Exo digestion

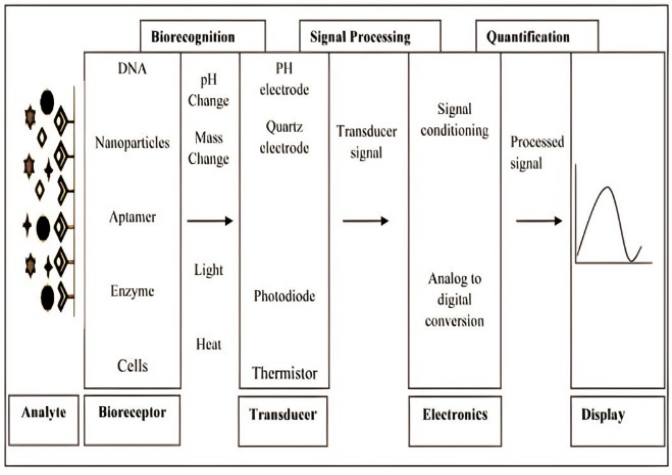

Figure 1: Elements of Biosensor.[4]

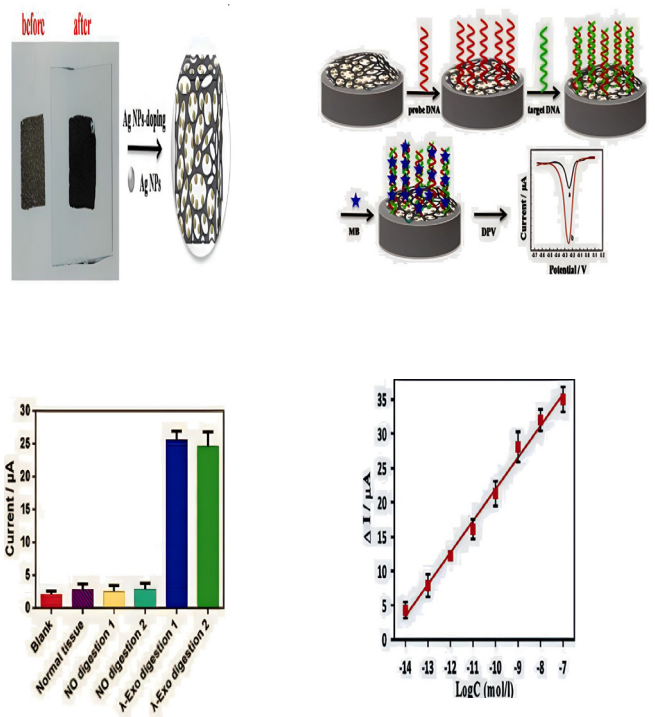

Figure 2: A, B, C.

Table 1: Studies related to some selected Enzyme based Biosensors.

Compound	Electrode type	Method	Enzyme	Sensitivity	Linear range	LOD	Application	References
Atrazine	MWCNTs/PVA-SPG/Tyr/SPE	CV	Tyrosinase	NS	0.5-20.0 ppm	0.3PPM	Water sample	39
Capsaicin	PAL/Nafion/MWCNTs/Pt-E	DPV	Phenylalanine ammonia- lyase enzyme	NS	NS	0.1863PPM	Real sample	40
Carbaryl	GCE/rGO/AChE	DPV	AchE	NS	NS	1.9 nM	Fruit sample	41
Catechol	Lac/GA/PANI/GCE	CV	Laccase	706.7mA.L moL^{-1}	$3.2* 10^{-6}$-$1.96* 10^{-5}$M	$2.07*10^{-6}$ M	Buffer	42
Catechol	Lac/ZnS: Ni/ZnS/GCE	CV	Laccase	NS	0.1-100 µM	35Nm	Water sample	43
Cholesterol	Ag/GO&CHER&CHOD/ AuNPs/SPE	LSV	CHOD CHER	0.084µAcm^{-2} ppm	0.01-5000 PPM	0.001PPM	Buffer	44
Cholesterol	ChEt-ChOx/ZnO-CuO/ITO/ Glass bioelectrode	CV	ChO_X ChEt	760mA cm^{-2} µM	0.5-12 Mm	NS	Human serum sample	45
D-Alanine	DAAO/PTCA/MWCNTs/GCE	CV	DAAO	NS	$1.0*10^{-8}$-$1.0*10^{-3}$ M	$3.3*10^{-9}$ M	Real sample	46

verifies the desired DNA creation. In order to corroborate the detection of LC, the CYFRA21-1 biomarker develops a stronger signal and peak current in the presence of the MB indicator with a linear relationship at various concentrations (of normal tissue). To identify these indicators(biomarkers), blotting, and PCR-based techniques are widely used.[26,27]

A) Preparation of 3D/AgNPs and detection process of target DNA

Amperometric response compared to λ-exo digestion to capture PCR product.

Peak current vs. log of the concentration of target ssDNA by linear regression equation: ΔI (μA) = 68.15 + 4.623 log C (M).

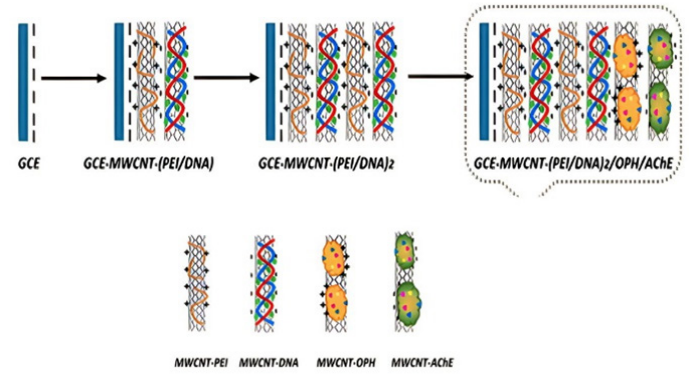

Figure 3: Identification of paraoxon as organophosphate and carbaryl as non-organophosphate compounds on GCE for the makeover of enzyme-based biosensor.

Table 2: Studies on selected Immunochemical Biosensors.

Biomarker	Type of illness	Immunosensor	Electrochemical technique	Linear range	LOD	References
PSA	Prostate	HRP-modified magnetic particles labelled anti-PSA antibodies. AuNPs-modified pyrolytic graphite disc electrode.	Amperometry	4-10 ng.mL^{-1}	0.5 pg.mL^{-1}	50
PSA	Prostate	Anti-PSA/MWCNTs/IL/GCE.	Differential pulse voltammetry	0.2-1.0 ng. mL^{-1} 1-40.0 ng. mL^{-1}	20 pg. mL^{-1}	51
PSA IL-6	Prostate Rheumatoid Arthritis Systemic Lupus Erythematosus	AuNPs-microfluidic 8-electrode SPCE array.	Amperometry	0.23pg.mL^{-1} PSA 0.30 pg. mL^{-1} IL-6	-	52
PSA hCG	Prostate Cancer Ovarian Testicular Trophoblastic Cancers	Porous membrane-coated 2-electrode gold array.	Amperometry	NS	0.4μg.L^{-1} PSA 2.5 UL^{-1} hCG	53
PSA IL-8	Prostate Rheumatoid Arthritis, Inflammatory Bowel Disease, Psoriasis, Acute Respiratory Distress Syndrome	16-electrode SPCE array.	Amperometry	-	5pg.mL^{-1} PSA 8 pg. mL^{-1} IL-8	54
PthA	Citrus Bacterial Cancer Disease	AuNP/PB/CILE/GCE.	Square wave voltammetry	0.03-100.00 nM	0.01nM	55
TNF-α	Rheumatoid Arthritis	PA+PAA/GCE.	Amperometry	0.02-200.00 ng.mL^{-1}	0.01ng.mL^{-1}	56

Biomarker	Type of illness	Immunosensor	Electrochemical technique	Linear range	LOD	References
TNF-α	Rheumatoid Arthritis	K3[Fe(CN)6]-CHT/GA/ NA/Mouse anti-human TNF-α	Cyclic voltammetry	0.02-34.00 ng.mL^{-1}	10.0 pg.mL^{-1}	57
TNF-α	Rheumatoid Arthritis	C60- fMWCNT-IL	Differential pulse voltammetry	5.0-75.00 pg.mL^{-1}	2.0 pg.mL^{-1}	58

Enzyme based Electrochemical Biosensor

In general, biosensors are categorized by the type of transducer they utilize or by the biological component they use, such as enzymes, nucleic acids, antibodies, or cells. Enzyme-based Electrochemical sensors are generally of low cost and show rapid results when compared to the other classic chromatographic and spectroscopic methods.[28] A biosensor is an appliance having a transducer and a sensing component built right in. A bioreceptor plus a transducer that generates a response proportional to the concentration of the target substance make up an enzyme biosensor.[29] Based on the quantity of the analyte, the enzyme preferentially interacts with the target analyte to produce an electrical signal. Leland C. Clark Jr.'s attempts to monitor oxygen in biological fluids markedly marked the beginning of the biosensor.[30]

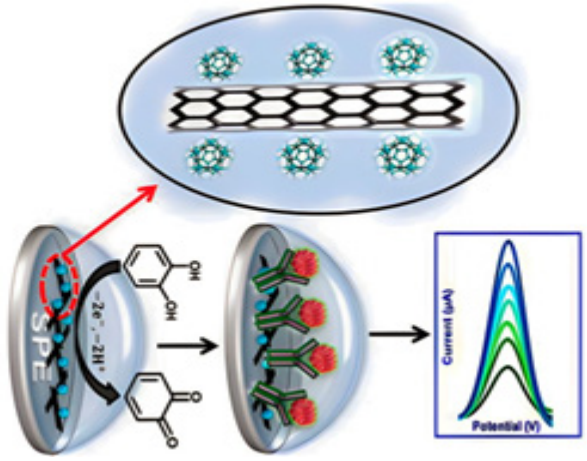

Figure 4: Diagrammatic illustration of label-free electrochemical immunosensor based on Fullerene-Functionalized Carbon Nanotubes/Ionic Liquid.

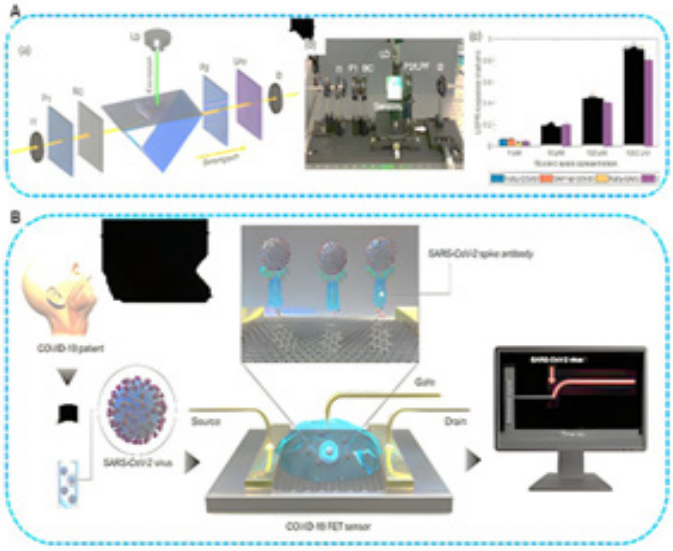

Figure 5: (A) (a) Pattern (b) experimental arrangement of multi-functional PPT enhanced LSPR biosensor, (c) Concentrations of several viral oligos measured using LSPR biosensor, (B) picture of FET-based biosensor.

In 1962, Clark proposed the idea of an enzyme-based instrument, which was realized as a clinical analyzer in 1975. The majority of conventional electrochemical enzyme biosensors are built around oxidoreductase enzymes and amperometric detection. An electrochemical setup is used to measure the redox, electron transfer process that occurs at the electrode surface and is related to the biocatalytic conversion of the target analyte. This electron transfer process generates current proportional to the amount of analyte present.[31,32]

Glucose, lactate, glutamate, urea, and cholesterol enzyme biosensors are the ones that are utilized the most in the clinical field. The analyte that has been investigated the most thoroughly is glucose. Due to its significance in the management of diabetes, it continues to get a great deal of recognition. This particular section concentrate on important progresses in enzyme-based biosensors, the majority of which have happened in the recent years. Commonly employed sensors for both practical and commercial application include glucose, lactate, and glutamate/ glutamine. The primary step in the makeup of enzyme based electrochemical biosensor is the enzyme immobilization. There are various ways to immobilize enzymes, including physical adsorption, covalent attachment, imprisonment, and other methods like Covalent crosslinking as well as encapsulation.[33-36] The literature's observations on the use of electrochemical enzymatic biosensors with applications are compiled in Table 1.

An electrochemical biosensor for the identification of organophosphorus pesticides was proposed by Zhang and colleagues on the basis of GCE-MWCNT–(PEI/DNA)2/ OPH/AChE.[37] On this sensor, the paraoxon responses were investigated using CV at a LOD of 0.5 μM. Using CV and UV-vis spectrophotometry, they reported on the production, optimization, and characterization of a biosensor (Figure 3).[38]

Immunosensor based Electrochemical Biosensors

A specific target analyte, Antigen (Ag), is detected by the creation of a stable immunocomplex between Antigen and Antibody as a capture agent (Ab), which produces a quantifiable signal provided by a transducer in an immunosensor, a type of affinity solid-state based biosensor.[47,48] An affinity biosensor known as an immunosensor relies on interactions between an antigen and a particular antigen that has been immobilised on a transducer surface. Depending on the type of signal, electrochemical immunosensors can be classified as amperometric, potentiometric, conductometric, or impedimetric based on computation of an electrical signal captured by an transducer. One of the immunoassay techniques is the immunosensors, which have all the fundamental performance features of immunoassays. The biological recognition area, the physico-chemical transducer, and the electrical impulse generator are the three components that make up the immunosensor.

Immunosensors can be created for heart illnesses, autoimmune diseases, cancer biomarkers, and more. A Label-Free Electrochemical Immunosensor for Detection of Tumor Necrosis Factor based on Fullerene-Functionalized Carbon Nanotubes/Ionic Liquid (C60-CNTs-IL) was created by Mazloum-Ardakani *et al.* in their paper (Figure 4). Additionally, the label-free electrochemical immunosensor that was developed proved successful. AFP, a biomarker for liver, ovarian, and testicular cancer, was discovered by Chen and colleagues using a one-step electrochemical immunoassay. The antigen-antibody complex was formed by the immobilisation of horseradish peroxidase-anti-AFP on a nanogold-functionalized graphene interface, and HRP was then used to catalyze the reduction of H_2O_2 in the solution. The Detection Limit (LOD) for AFP was 0.05 ng/mL, with a linear range of 0.1-200 ng/mL.[49]

Besides in here, we provide an update on the electrochemical immunosensors used in clinical study as of recent publications (Table 2).

OPTICAL BIOSENSORS

In order to perform a qualitative and quantitative analysis of the target, the optical sensors primarily examine the optical signals produced when target and the detection element are combined. They then directly transform these signals through transducer in real-time. They are widely employed in various fields because of their accuracy, simplicity of maintenance and quick detection.[59]

The 2019 Coronavirus Disease (COVID-19) outbreak for one more time highlighted importance in creating swift and extremely sensible diagnostic methods for fast detection of patients who are infected.

Despite sensitivity and specificity requirements being met RT-PCR diagnostic procedures, there are certain inherent drawbacks with time-consuming.

Its application possibilities are restricted by sophisticated machinery and experienced operators. Optical biosensors based on nanomaterials attracted a lot of attention for the detection of SARS-CoV-2. The development of optical biosensors for SARS-CoV-2 diagnosis, including colorimetric, Electrochemical (EC), Quartz Crystal Microbalance (QCM), Field Effect Transistor (FET)-based, localized surface plasmon resonance (LSPR), Surface Enhanced Raman Scattering (SERS), and fluorescence-based biosensors.[60,61] However, LSPR, FET, EC, and SERS biosensors have been used often in pandemic which is mainly highlighted in the below article.

Plasmonic Biosensors

In both life science and pharmaceutical research, these biosensors play an important role in characterizing and measuring bio-analytical targets. These biosensors are very sensitive, devoid of tagging which are suitable for a variety of therapeutically relevant analytes that are present to be targeted. These are utilized to identify SARS-CoV antibodies using a macromolecule of amino acids made by combining a SARS coronaviral surface antigen with gold-binding polypeptides in a genetical format.[62]

Viral antibodies can be found at the nanomolar level. The bioassay was performed using a portable SPR device. In order to identify patients who have been inoculated against SARS-CoV-2 and strategically help vaccine development efforts, the immune system responds to the sensor's exposure to SARSCoV-2 by producing antibodies at levels that can be identified and tracked. By precisely identifying the antibodies, we can support the creation of the vaccine and assess those who have developed immunity to SARS-CoV-2.[63]

The multi-functional plasmonic biosensor built by the joint effects of Plasmonic Photothermal (PPT) and Localized Surface Plasmon Resonance (LSPR) has also been shown by Wang's research team to have encouraging COVID-19 diagnosing capabilities. By hybridizing nucleic acid, two-dimensional gold Nanoislands (AuNIs) and complementary DNA receptors may identify specific sequence from virus, as shown in Figure 5A. The creation of plasmonic heat on the same surface of the AuNIs when they began shining at their plasmonic resonance frequency greatly improved detecting capabilities. The *in situ* hybridization temperature can be raised by the locally generated PPT heat, which then permits differentiation of two identical gene sequences. In identification of specific virus, our multi functionalized LSPR sensor has demonstrated excellent sensing capability.[64]

FET based Biosensors

Field-effect transistor dependent biosensing platforms provide wide range of intriguing advantages compared to current diagnostic methods, including the capability of being extremely accurate and to instantaneously identify low volume containing analytes. These could be used for point-of-care assays, clinical

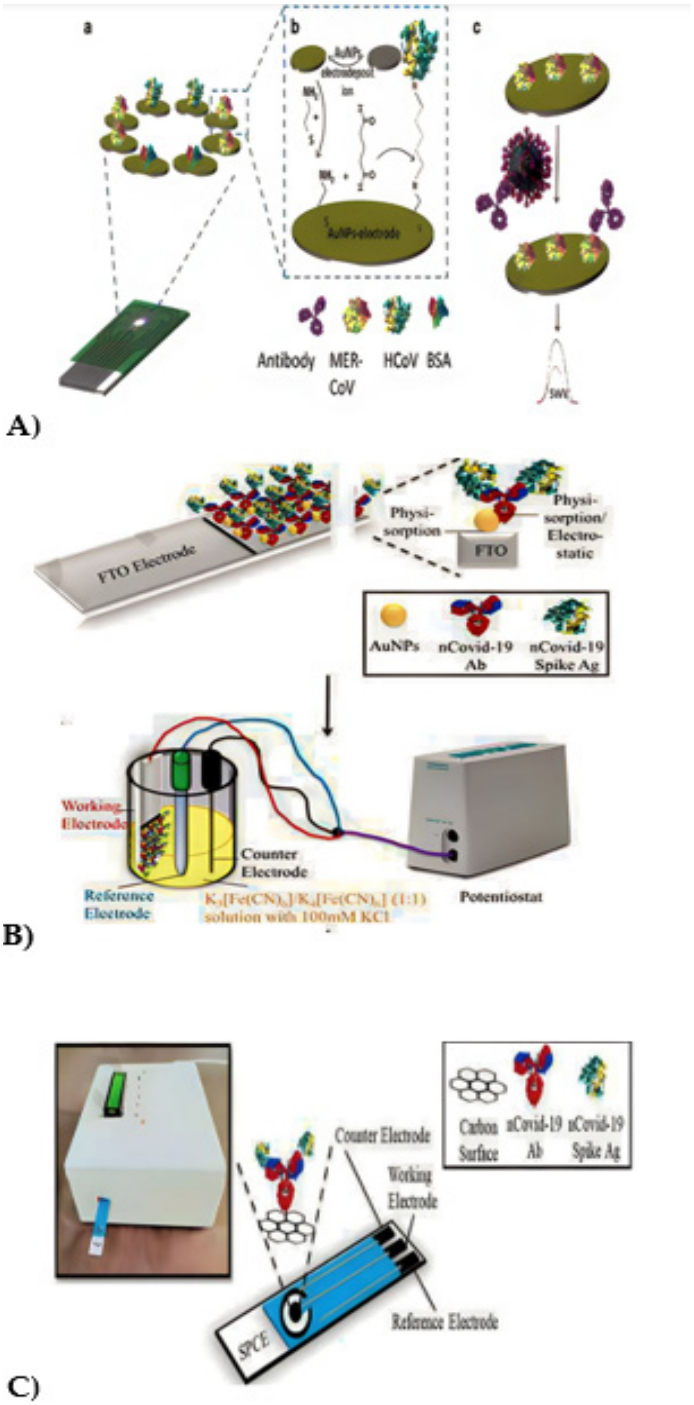

Figure 6: (A) Chip array, immunosensor fabrication process and virus identification (B) FTO electrode modification process (C) Diagram of electrochemical eCovSens device.

analysis, and on-site diagnostics.[65] Due to its capacity to detect adjacent surface fluctuations and serve as an ideal sensing platform, graphene, which has carbon atoms of hexagonal orientation exposed on its surface and is electronically conductive, high charge mobility has proven to be extremely detectable in sensing systems. So these graphene-based FET biosensors are crucial for performing highly sensitive immunological diagnosis. A system depending on this phenomenon for identifying the coronavirus in clinical specimens has been successfully created by Sea and colleagues as illustrated in Figure 5B.[66] In order to create the biosensor, the graphene sheets of the FET were coupled with particular antibodies against the SARS-CoV-2 spike protein. Antigen protein, a self-cultured virus, and nasopharyngeal swab samples from COVID-19 pneumonia patients were used to assess the biosensor's sensing capacity.

The SARSCoV-2 spike protein could be detected by the FET biosensor at 1 fg/mL in phosphate-buffer saline and 100 fg/mL in clinical transport medium.

EC Biosensors

Because of its simplicity, low cost, ease of downsizing, and ability to be manufactured in large quantities, electrochemical biosensors have drawn the interest of scientists. Additionally, they can be used at the point of care in clinics or at homes.[67,68] Early diagnosis is the sole method for controlling and combating the COVID-19 virus since there is no vaccination or specialized medication available for its treatment. Figure 6A shows the architecture of a multiplexed electrode array. The created EC sensor successfully used in spiked nasal samples, and influenza A and B did not cause any measurable interference. Patricia Abad-Valle and colleagues created a further straightforward, affordable, and user-friendly EC Geno sensor on gold films for the detection of the SARS-CoV gene. Square wave voltammetry was used by the Geno sensor to reach a response criterion of 6 pM for sequencing this DNA.[69]

Gandhi's research team has created a custom made biosensing device (eCovSens) that is available for purchase to diagnose COVID-19 Ag. In order to create a potentiostatic biosensor, a Fluorine-doped Tin Oxide electrode (FTO) was embellished with AuNPs and bound with the COVID-19 Ab as shown in Figure 6B. Screen printed carbon electrode was immobilized with COVID-19 Ab to analyse the difference in conductivity, shown in picture 6C, in order to build eCovSens.[70] Both the FTO immunosensor and the SPCE biosensor shown exceptional detection in the region ranging 1 fM to 1 M for COVID-19 Ag detection. In spiked saliva specimens, the detection limits for the eCovSens and potentiostatic devices were 90 fM and 120 fM, respectively. Within 10–30 s, the eCovSens gadget as-fabricated can detect COVID-19 Ag. Because of its improved selectivity and specificity, this platform can be utilized as a backup diagnostic tool to find COVID Silver traces in saliva from patients. The eCovSens gadget can be a useful diagnostic tool because it is highly affordable, portable, needs very little electricity (1.3-3 V), and can even be powered by batteries.

SERS-based Biosensors

The accurate measurement of analyte utilizing Surface Enhanced Raman Scattering-coded nano particles by replacing colloidal gold to detect response has drawn the researchers' undivided

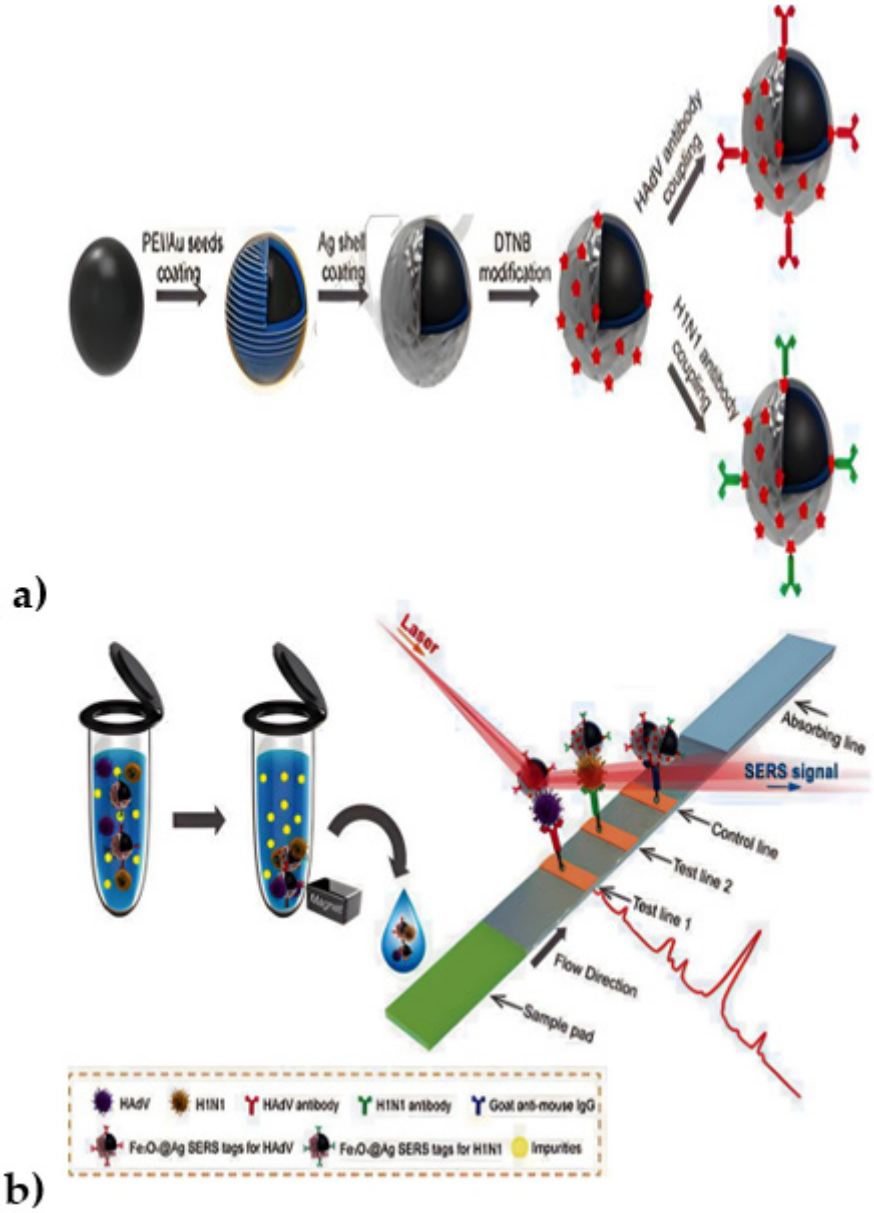

Figure 7: (a) Antibody-modified Fe_3O_4@Ag nanotags preparation, (b) Brief illustration of magnetic SERS-based biosensor for the identification of respiratory viruses.

attention to SERS-based biosensors. SERS tags consist 3 main parts: an Gold/Silver nanoparticle that serves as a Raman enhanced substrate, adsorbed Raman reporter dyes that generate distinctive Surface Enhanced Raman Scattering response, and certain antibodies that bind targets. Figure 7 illustrates how Wang *et al.* constructed a Surface Enhanced Raman Scattering dependent biosensor to concurrently identify the presence of two viruses, such as Influenza A (H1N1) and Human Adenovirus (HAdV), using Fe_3O_4@Ag nanoparticles as magnetic SERS nanotags.[71] For H1N1 and HAdV, respectively, the small amounts of detection calculated using SERS-based biosensors were 50.0 pfu/mL and 10.0 pfu/mL. The biosensor's sensitivity was 2000 times greater than that of the widely used colloidal gold strip approach. Without any pretreatment, the suggested biosensor can be used directly for the examination of living material. Additionally, a porous carbon substrate coated with Ag nanoparticles was used to build a SERS-based biosensor for the detection of three distinct viral types.[72] For these three viruses, the lowest feasible concentration that our biosensor could detect was 1 107 copies/mL. The distinction of virus was made possible by the SERS spectra.

CONCLUSION

Biosensor technology has a number of distinct and significant advantages over conventional analytical techniques, including real-time operation, low limits of detection, greater sensitivity, decreased cost, simple operation, and downsizing. Without

prior separation or derivatization, simultaneous detection and quantification are possible. This review illustrated the diverse range of applications for electroanalytical biosensors. Despite the increased use of disposable electrodes, change in electrodes has received more attention because of larger surface area. The approval processes prove that they work with actual samples. Biosensors based on DNA could be used to examine medication interactions, analyze genes, and perform hybridization. Researchers have favored voltammetric and amperometric methods. Immunosensors are utilized in the detection in addition to the measurement of variable range of samples as a result of the quick development of immunological agents and technology. Wider applications of simple, affordable, and dependable immunosensing devices have been developed, including extensive screening programs. Electrochemical biosensor research has been expanding in recent years. Electrochemical biosensors will soon be used more extensively in the medical fields among others. Furthermore, the development of electrochemical biosensors is intimately tied to wireless real-time data collecting. Biosensors and biochips are tools that can be used at the Point of Care (POC). Information regarding potential future developments in molecular diagnostics will be provided through the improvement of DNA biosensor. It is conceivable that PCR-free DNA biosensors will soon be available thanks to the industry's rapid advancements in electrochemical biosensing.

Since the pandemic's start, spread of coronavirus has been witnessed throughout the world. Additionally, the virus is always evolving in a sneakier way, posing issues with temporal persistence and globalization. To stop the spread of viruses, it is crucial to create technologies for quick virus detection and diagnosis. An excellent option for the identifying this virus is optical biosensors. The significance of these biosensors is particularly stressed in the detection of coronavirus. For asymptomatic patients, everyone should have easy access to in-house biosensor instruments in detection of virus in people. Their capacity to detect the target virus antigen quickly, on-site, and with great sensitivity can ultimately lead to an faster detection of covid. In addition to the busiest places, including airports and hospitals, they can scan people there. In order to detect viruses, the use of nanoparticles in conjunction with electrochemical diagnostic techniques is promising. Nanomaterials and nanotechnologies should evolve in order to create better biosensors that can detect virus antigens with good sensitivity and selectivity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AchE: Acetylcholinesterase; **AuNPs:** Gold Nanoparticles; **CEA:** Carcinoembryonic antigen; **CV:** Cyclic Voltammetry; **CHER:** Cholesterol Esterase; **ChOX:** Cholesterol oxidase; **DPV:** Differential Pulse Voltammetry; **GPO:** Glycerol-3-Posphate Oxidase; **GA:** Glutaraldehyde; **GK:** Glycerol kinase; **GOX:** Glucose Oxidase; **HRP:** Horseradish peroxidase; **hcG:** Human chronic Gonadotropin; **PtE:** Platinum electrode; **MWCNT:** Multi-walled Carbon Nanotube; **PEI:** Polyethyleneimine; **PSA:** Prostate-Specific-Antigen; **PVA:** Polyvinylalcohol; **QDs:** Quantum Dots; **TNF-α:** Tumor necrosis factor alpha; **ZnONRs:** Zinc oxide nanorods.

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