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Biosensors–The Point of Care Diagnostics (POCD): A Review

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ABSTRACT

Recent advances in biosensors have significantly enhanced point-of-care diagnostics (POCD). These biosensors are crucial for the quick identification of diseases at or near the location of the patient. This of course helps in speedier medical judgments and better health results. Several label-free biosensors have been developed, including electrochemical, surface plasmon resonance, and white light reflectance spectroscopy. These devices getting improved due to complementary technologies like microfluidics, lab-on-a-chip, and device automation. POCD biosensors are used to detect pathogens, antigens, and biomarkers from biological samples like blood, urine, and saliva. The global POCT market is rapidly growing, driven by the need for quick and accurate diagnostics. This paper reviews the principles underlying biosensor technology and highlights recent advancements in sensor design, signal transduction mechanisms, and integration with microfluidic platforms. The critical role of biosensors in detecting biomarkers for illnesses like cancer, metabolic problems, and infectious diseases is examined, as well as how they could affect patient care and clinical results. Challenges and future directions in Biosensor Development for POCD are also addressed, emphasizing the need for enhanced sensitivity, specificity, and multiplexing capabilities to meet the evolving demands of modern healthcare. These developments are opening the door for more effective, portable, and user-friendly POCDs in the future.

Key-words: Biosensors, Point of care diagnostics, Infectious diseases, dengue, Transducer, Electrochemical

INTRODUCTION

The slogan-Health is wealth advocates that ill health is an important contributor to Socioeconomic status and welfare. Infectious diseases have always had a big influence on health status globally in recent years. The agents of much debate are the viruses. Viruses have a devastating impact on people's health everywhere. It is now more crucial than ever to identify this virus to stop the spread of viral infections and protect people from their harmful effects. Accurate and timely diagnosis is crucial to impede the progression of a disease and break the chain of transmission. Conventional diagnostic techniques are typically time-consuming and costly, making them inefficient for early diagnosis of infections and inconvenient for use at the point of care [1].

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Emerging trends in the field of biotechnology have dramatically contributed to the development of diagnostic tools with improved sensitivity and accuracy. These technologies undoubtedly aid clinicians in the early diagnosis and treatment of various conditions. One of such advances is the development of biosensors. Biosensors have several applications in the medical field, such as monitoring glucose levels in diabetic patients, detection of pathogens and toxic metabolites, as well as measurement of Folic acid, Biotin, Vitamin B_{12}, and Pantothenic acid etc [2]. Biosensors have also become more useful in the veterinary sector [3–9].

Biosensor- A biosensor is a cutting-edge analytical tool that incorporates a biological constituent with a physical detector. It is comprised of a transducer, a detector with a digital output, and a sensing bioreceptor.

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A biosensor is, by definition, a self-contained analytical instrument designed to detect (reversibly and selectively) the concentration or activity of chemical species in any sample. It consists of biologically active material in close contact with an appropriate transduction element [10–21].

Analytical devices known as biosensors selectively interact with analytes using biological material. A transducer detects and converts the observable physical change that arises from this interaction into an electrical signal. After that, the electrical signal is amplified, encoded, and displayed as the analyte concentration of the preparation or solution. An analyte is a substance whose concentration the biosensor is going to measure in this instance [22].

The first biosensor was invented in 1962 by LC Clark and C. Lyons. Many reviews have been published on the principles and applications of biosensors using enzymes [10,23–32]. The six components that make up a biosensor are the signal processor, signal amplifier, electrochemically active interface, transduction element, bioreceptor, and display. After attaching itself to the immobilized biological material, the analyte produces a product. The transducer then transforms the product-linked changes into electric signals so that the detector can measure, amplify, and read them out. The values are shown on the monitor and controlling system after processing. Based on its transduction element (electrochemical, electric, optical, piezoelectric, and thermal) or biorecognition element (antibody [Ab], enzymes, nucleic acids, and whole cells), biosensors are divided into many categories. Most of these biosensors are POCDs, or point-of-care diagnostic assays, which offer the results without requiring the use of laboratory personnel or equipment. Proteins, nucleic acids, metabolites, medications, dissolved ions and gasses, human cells, and microorganisms are among the analytical "targets." Blood, saliva, urine, and other physiological fluids or (semi)solids are examples [33]. Thus, a biosensor is an independent, integrated device that uses a biological recognition element in close spatial proximity to a transducer element to provide precise quantitative or semi-quantitative analytical information (Fig. 1 & 2).

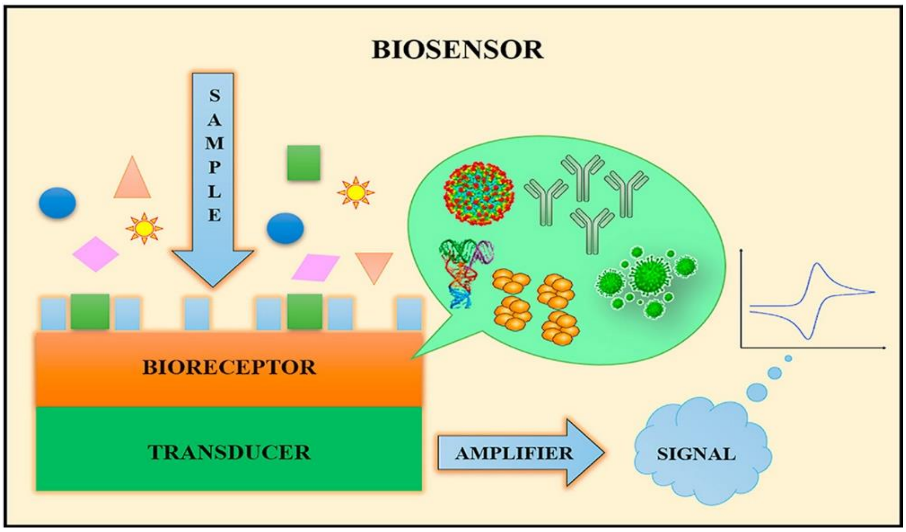

Fig. 1: Simplified overview of a Biosensor [34].

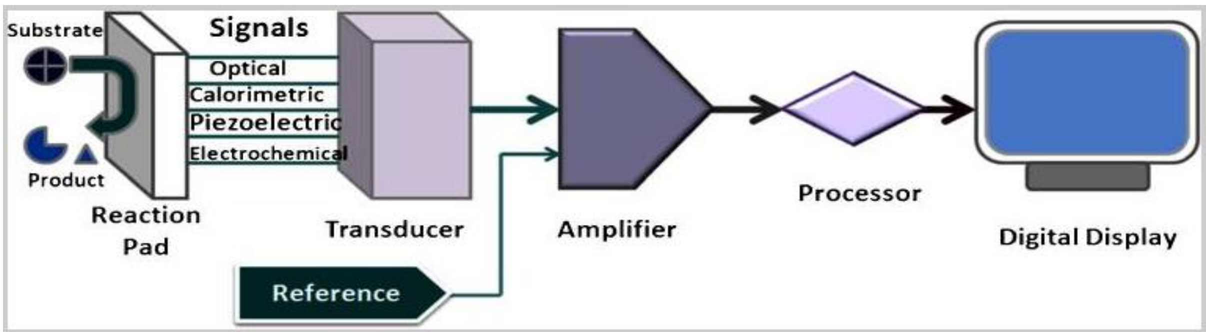

Fig. 2: Design and Principle of a biosensor.

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A sensor is defined as a device or module that aids in detecting changes in physical quantities, such as pressure, heat, humidity, movement, force, and an electrical quantity, like current, and thereby converts these to signals that can be detected and analyzed. A transducer is defined as a device that can convert energy from one form to another [35].

Types of Biosensors- The biosensors are of 5 types:
(i) Calorimetric
(ii) Potentiometric
(iii) Amperometric
(iv) Optical and
(v) Acoustic wave biosensors

Below is a quick description of these biosensors' main features:

- Heat released from the process or heat absorbed (Calorimetric biosensors)
- Modifications to electrical or electronic output (biosensors that use electrochemistry).
- Biosensors that use amperometric redox reactions
- Optical biosensors measure the difference in light output or light absorbance between the reactants and products.
- determined by the mass of the products or reactants (Piezo-electric biosensors)

Due to its exceptional qualities, including high sensitivity, portability, low cost, simplicity of instrumentation, and ease of use, electrochemical detection is one of the most promising detection techniques for biosensing applications among the various transducers used to date. It represents most published works in this field [36].

Point-of-care biosensors- The biosensors have proved to be an essential portable point-of-care instrument. It reduces the diagnosis time. The field of biosensors spans a wide range of detection principles, with notable examples including electrochemical, optical, and molecular-based sensors. Each type possesses distinct advantages suited to different diagnostic needs, from the high sensitivity and low-cost operation of electrochemical sensors to the precision and multiplexing capabilities of optical sensors. These technologies are increasingly integrated into portable and user-friendly devices, facilitating their deployment in resource-limited settings and non-clinical environments where immediate diagnosis is critical [37,38].
POCT is one of the most significant uses of biosensors. The primary objective of this review is to comprehensively explore the current state-of-the-art biosensor technology applied specifically to point-of-care diagnostics.

Need for POC testing- Several laboratories are pursuing work on upgrading the biosensors. One of the aspects is to have a miniaturised portable gadget [39]. This avoids the transport of the sample to the laboratory. To identify environmental contaminants, quick, on-site, and inexpensive testing techniques are required [40]. POCT technology is becoming more and more significant in viral screening and detection due to its advantages [41]. Many metabolites of diagnostic importance are tested, such as cotinine (the primary metabolite of nicotine). It has become global to ameliorate the COVID pandemic due to the availability of huge amounts of such POC kits so that the program implementation and performance were successful [24,42,43].
To deliver quick findings, POCT involves doing a diagnostic or prognostic test close to the patient. This means the test itself must be simple to conduct quickly and without the need for sophisticated or expensive equipment. The true origin and character of any disease are determined by early and accurate diagnosis. These days, the primary emphasis is being placed on early disease detection to efficiently manage treatment, decreasing the patient's death rates.

Electrochemical biosensors- An electrochemical transducer is used by electrochemical biosensors, a particular kind of biosensor, to transform a biological recognition event into an electrical signal. Their great sensitivity, quick reaction, and capacity to be reduced in size for portable devices make them commonly employed. POCD is a promising tool in the field of early detection because of its capacity to produce rapid results in no laboratory settings, which supports patient-centred approaches to healthcare delivery [44].

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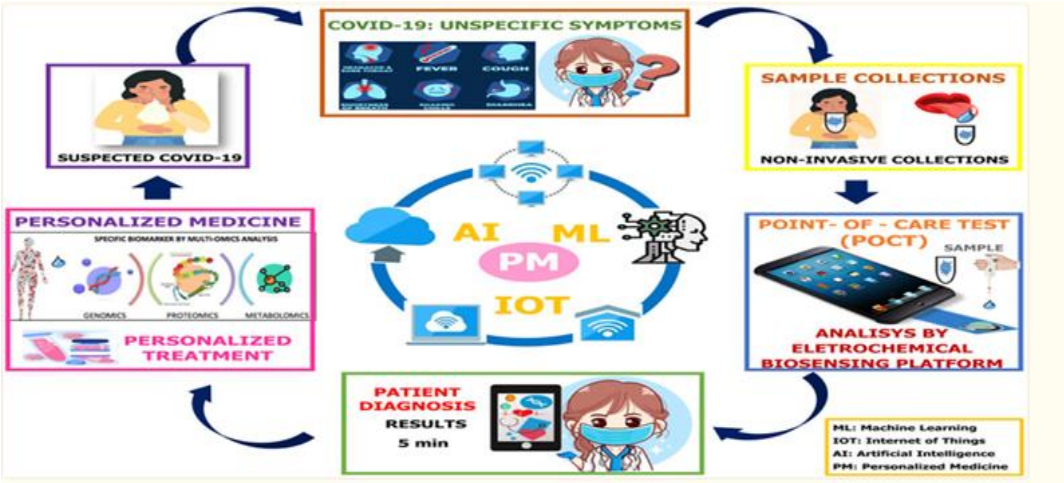

Fig. 3: Conceptual diagram depicting the electrochemical biosensing platforms and how these are employed in the most remote and resource-poor areas and that is how they are the best point-of-care diagnostic instruments for pandemic situations [44]

Electrochemical Biosensors have the following main components:

Biological Recognition Element (Bio receptor) which specifically interacts with the target analyte (e.g., glucose, DNA, antibodies). The interaction between the bio-receptor and the analyte generates a biochemical signal.

Transducer, which converts the biochemical signal into an electrical signal that can be measured.

Electrode, where the biological recognition element is immobilized. The electrode can be made of materials like gold, platinum, or carbon, depending on the specific application and transduction mechanism.

Signal Processing and Output, where the electrical signal generated by the transducer is processed and interpreted to determine the concentration or presence of the analyte. This signal can be displayed on a screen, recorded digitally, or interpreted by an algorithm.

Advantages of Electrochemical Biosensors

- ✓ **High Sensitivity**- They can detect very low concentrations of analytes.
- ✓ **Rapid Response**- They provide results quickly, often in real-time.
- ✓ **Miniaturization**- Suitable for portable and point-of-care applications.
- ✓ **Specificity**- The bio-receptor provides high specificity towards the target analyte.

Applications of Electrochemical Biosensors

Medical Diagnostics- These are used to monitor glucose levels (important in diabetes management), detect pathogens, or monitor biomarkers. Rapid and targeted disease detection is essential for early diagnosis and precise epidemiological surveillance in basic healthcare. A growing body of research and commercially available POCTs are essential for prompt and efficient response to infectious disease outbreaks, which in turn reduces pathogen spread and the number of afflicted individuals [45].

Electrochemical biosensors for dengue detection have be come the overwhelming method of choice among researchers due to their ability to be highly quantitative and qualitative.

A prime example of this technology is the glucometer, for which *Clark et al*. first presented the general idea in 1962. A glucometer is a glucose test strip that is connected to a pocket-sized amperometric transducer and is based on screen-printed electrodes that have been altered to include a particular enzyme as a biorecognition element. In the past few decades, these devices have dominated the diabetes monitoring industry due to their affordability and widespread use among patients and healthcare professionals in laboratories and at home. The glucometer's effectiveness as an analytical tool catalyzes the creation of novel POC electrochemical biosensing instruments with potential uses in cancer diagnosis and other fields [36]. Electrochemical Biosensor Technology is at the forefront of the development of POC devices [47].

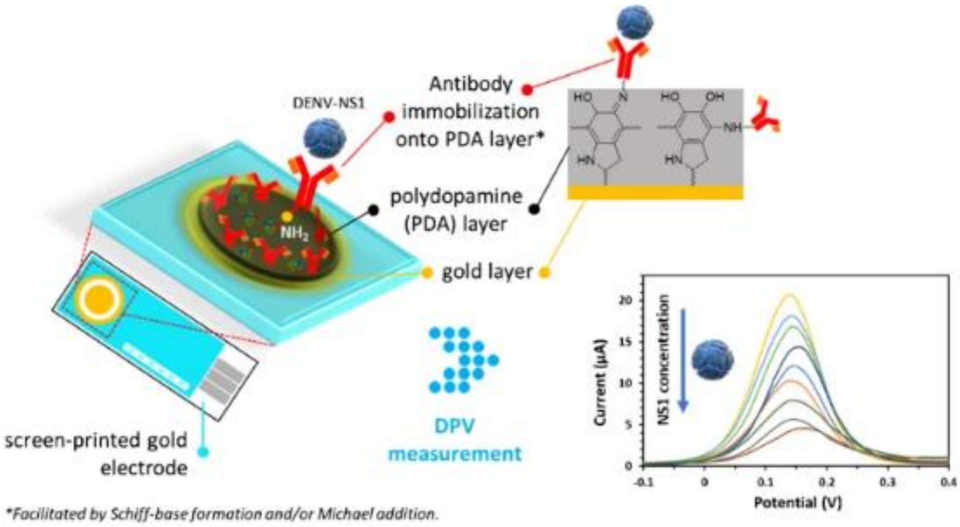

Fig. 4: The facile and versatile method of polydopamine (PDA) coating onto the surface of screen-printed gold electrodes (SPGEs) for a miniaturized point-of-care (PoC) detection device to detect dengue infection [46].

The Electrochemical biosensing platforms have emerged as a boon for disease identification [48]. The electrode is the most vital component of an electrochemical biosensor [49].

Molecularly imprinted polymers- Molecularly imprinted polymers (MIPs) are artificial materials that preferentially attach to target molecules to replicate the action of natural antibodies and receptors. They are made by a procedure called molecular imprinting, in which monomers are polymerized around a target molecule or template. Then, the template is removed, leaving behind cavities that are chemically and morphologically complementary to the target molecule.

Characteristics of MIPs

Selective Binding- MIPs exhibit high selectivity towards the target molecule due to the specific recognition sites (cavities) that are molecularly imprinted during synthesis.

Versatility- They can be designed to recognize a wide range of target molecules, including small organic molecules, peptides, proteins, and even complex structures like viruses.

Stability- MIPs are generally stable under a wide range of conditions (temperature, pH, etc.), making them suitable for various applications.

Ease of Production- Compared to antibodies, MIPs can be synthesized relatively easily and cost-effectively in large quantities.

Because of their great chemical and physical durability, MIPs are a desirable substitute for receptors as recognition elements for biosensing [1]. They are fascinating because they can be tailored to recognize specific molecules, making them useful in various applications like sensors, drug delivery, and separation processes. To create MIPs, functional monomers must polymerize while the target molecules are present. Target molecules operate as templates during polymerization, interacting with the monomers through their functional groups to form a three-dimensional (3D) polymer surrounding the templates. Recognition cavities are produced when the templates are removed from the MIP matrix. These cavities match the templates in terms of functional group placement, size, and shape. These recognition holes can provide specific binding locations where target molecules can rebind to the MIP through interactions between complementary functional groups.

The coverings or molecules with great selectivity, such as enzymes or antibodies, are crucial for biology, chemistry, and diagnostics. These natural sensors might be costly or challenging. Furthermore, since they are biomolecules, their lifetime and applicability are limited. One method created to get around these restrictions is molecular imprinting. All that needs to be done to create imprints with specific selectivity is to polymerize a prepolymer in the presence of the target molecule.

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Two things take place at the same time when the polymer cures. Initially, the prepolymer's functional groups align themselves with their counterparts in the template. MIP-based biosensors have been generated for different templates ranging from molecules to proteins, viruses, and even entire cells [50]. Among the technologies used for building specific recognition properties, MIPs are attracting much attention [51].

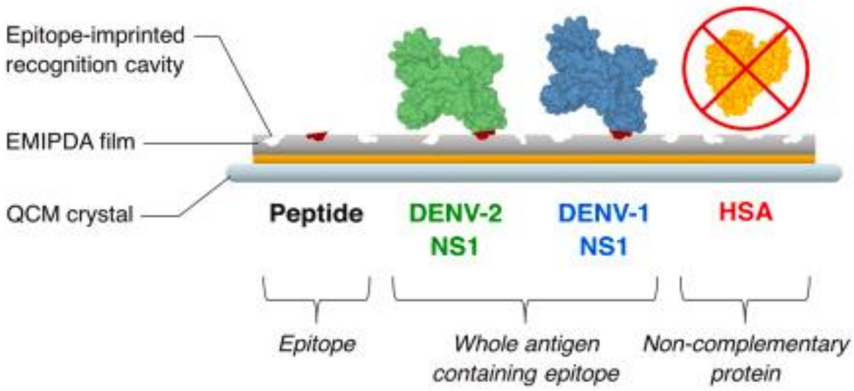

Fig. 2: Polydopamine-based sensing film imprinted with the dengue virus non-structural 1 antigen at a specific location for early dengue detection and prognosis. This technology has been adopted in dengue point-of-care diagnostics Source [52].

Comparative Analysis with Conventional Methods- Advantages of Biosensors over Conventional Techniques- Biosensors have seen significant advancements in 2024, offering several advantages over conventional techniques.

Advantages of Biosensors over Conventional Methods- Provide rapid detection and real-time monitoring, significantly reducing the time required for analysis [53]. They exhibit high sensitivity and specificity and can detect low concentrations of analytes with minimal interference [54]. Typically, compact and portable, allowing for on-site testing and POCD. It can be more cost-effective in the long run due to reduced reagent use, lower labor costs, and faster turnaround times. Easily integrated with digital systems for automated data collection and analysis, enhancing accuracy and efficiency.

CONCLUSIONS

Forthcoming developments in Nano-biosensors are to be oriented towards identifying and treating the diseases at the precise molecular targets. Relatively short time result announcement of biosensor and their miniaturization are all the plus points. Electrochemical biosensors are emerging as new gadgets -opted for by many clinical, toxicological, and food fields, with more companies investing in these technologies.

CONTRIBUTION OF AUTHORS

Research concept- Ashoka CH, Usha Saraswathi U
Research design- Ashoka CH, Usha Saraswathi U
Supervision- Ashoka CH, Usha Saraswathi U
Materials- Ashoka CH, Usha Saraswathi U
Data collection- Ashoka CH, Usha Saraswathi U
Data analysis and Interpretation- Ashoka CH, Usha Saraswathi U
Literature search- Ashoka CH, Usha Saraswathi U
Writing article- Ashoka CH, Usha Saraswathi U
Critical review- Ashoka CH, Usha Saraswathi U
Article editing- Ashoka CH, Usha Saraswathi U
Final approval- Ashoka CH, Usha Saraswathi U

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