Journal of Scientific Research in Allied Sciences
ISSN NO. 2455-5800
DOI No. 10.26838/JUSRES.2022.8.1.516
Contents available at www.jusres.com

BIOSENSORS: ROLE IN PHARMACEUTICAL SCIENCES (CURRENT & FURTHER SCENARIO)

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ARTICLE INFO

Article History
Received: Dec 2021
Accepted: Feb 2021
Keywords:
Biosensor, Pharmaceutical Technology, detector, health.

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ABSTRACT

REVIEW ARTICLE

Biosensors are analytical devices used for analyzing and detecting a chemical substance by combining a biological component with a physicochemical detector. Research sciences and medical societies have recently shifted into using cost-effective biosensors to test food & water contaminants, control human biologic processes, assess precise health diagnoses, and more. Researchers and medical practitioners need safe and cheaper means of performing their research, ensuring public safety, and delivering customized health options to patients. One such solution can be easily carried out by using biosensors. In the new medical field, biomedical studies of diagnosis are of growing significance. Biosensors' applications are for screening infectious to early detection, chronic disease treatment, health management, and well-being surveillance. Improved biosensors technology qualities allow the ability to detect disease and track the body's response to care. Sensor technology is integral to numerous, low-cost, and improved-form factors feasible in modern medical devices. Biosensors have good potential, as it is easy, scalable, and effective in manufacturing processes. This review gives a comprehensive description of the Biosensors applications in the medical field, Biotechnological Applications of Electrochemical Biosensors, current trends in biosensor research and development, and Emerging Technology in the Pharmaceutical Industry.

INTRODUCTION

Biosensors can be defined as, analytical devices consisting of a sensitive biological element and a physical detector element it is also called transducers coupled to an input/ output device. By the given definition, a biosensor is a self-contained integrated system, in which the detector determines an analyte of biological interest selectively and quantitatively with the help of a bio-receptor element also known as a bio-recognition element and a signal transduction element. A biosensor is a device and it has the properties which can detect, record, and transmit information regarding a physiological change or the presence of various chemical or biological materials. These biological materials may include enzymes, tissues, microorganisms, antibodies, cell receptors, and biologically derived materials too. The biosensor is a device that combines with a biological recognition element with a physical or chemical transducer to detect a biological product. More technically, the biosensor is a probe that combines with a biological one with an electronic component to yield a measurable

signal as a product. Biosensors are currently enjoying an ever ever-increasing in a wide variety of applications and therefore are important that students and scientists in the analytical arena are aware of the range of available biosensors, the principal they are based and, most importantly, their advantages and limitations. Biosensors represent promising analytical tools applicable in numerous fields areas like in food industry, clinical diagnosis, environment monitoring and other fields, where rapid and reliable analyses are needed. Some biosensors were successfully implemented in the commercial sphere, but the majority needs to be developed to overcome some imperfections. [1]

Category of Biosensor:

Electrochemical biosensors: Electrochemical biosensors are normally based on enzymatic catalysis of a reaction that produces or consumes electrons. The sensor substrate usually contains three electrodes; a reference electrode, a working electrode and a counter electrode. The target analyte is involved in the reaction that takes place on the active electrode surface, and the reaction may cause either electron transfer across the double layer (producing a current) or can contribute to the double layer potential (producing a voltage). We can either measure the current (rate of flow of electrons is now proportional to the analyte concentration) at a fixed potential or the potential can be measured at zero current (this gives a logarithmic response).

Note that the potential of the working or active electrode is space charge sensitive and this is often used (Biosensors Primer). Another example, the potentiometric biosensor, (potential produced at zero current) gives a logarithmic response with a high dynamic range. Such biosensors are often made by screen printing the electrode patterns on a plastic substrate, coated with a conducting polymer and then some protein (enzyme or antibody) is attached. They have only two electrodes and are extremely sensitive and robust. They enable the detection of analytes at levels previously only achievable by HPLC and LC/MS and without rigorous sample preparation. All biosensors usually involve minimal sample preparation as the biological sensing component is highly selective for the analyte concerned. The signal is produced by electrochemical and physical changes in the conducting polymer layer due to changes occurring at the surface of the sensor. Such changes can be attributed to ionic strength, pH, hydration and redox reactions, and the latter due to the enzyme label turning over a substrate 2

ICS biosensors: An Ion Channel Switch (ICS) biosensor can be created using gramicidin, a dimeric peptide channel, in a tethered bilayer membrane 20. One peptide of gramicidin, with an attached antibody, is mobile and one is fixed. Breaking the dimer stops the ionic current through the membrane. The magnitude of the change in electrical signal is greatly increased by separating the membrane from the metal surface using a hydrophilic spacer. Quantitative detection of an extensive class of target species, including proteins, bacteria, drug,s and toxins has been demonstrated using different membrane and capture configurations

Microbial biosensors: Using biological engineering researchers have created many microbial biosensors. An example is the arsenic biosensor. To detect arsenic they use the Ars operon

Plasmonic biosensors The surface plasmonic resonance (SPR) biosensors are now essential tools and have obtained the key role in characterizing and quantifying bio-analytical targets both in life science and pharmaceutical research. These biosensors are label-free, highly sensitive, and can be applied to different types of clinically interesting target analytes. The SPR biosensors have also been used for the detection of antibodiesody of SARS-CoV using a protein which was created by genetically fusing gold binding polypeptides to a SARS coronaviral surface antigen [8]. Recently, Masson's research group has reported the use of human serum samples without dilution for the detection of nucleocapsid antibodies which are specific against the SARS-CoV-2 employing SPR biosensing technology [9]. The peptide monolayer was successfully coated on SPR biosensor and further functionalized with virus

nucleocapsid protein which was finally able to detect SARS-CoV-2 antibodies at the nanomolar level. The portable SPR instrument was used to carry out the bioassay. The working mechanism is that when the sensor is exposed SARS-CoVS CoV- 2, the immune system gave response by expressing antibodies at that which can be detected and monitored to find out the patients immunized against SARS-CoV-2 and support the efforts for vaccine development strategically. By exactly detecting the antibodies, we can assist the vaccine development and evaluation of individuals that have become immune to SARS-CoV- 2. Moreover, Wang's research group has demonstrated that the dual-functional plasmonic biosensor construed up using combined effects of plasmonic photothermal (PPT) and localized surface plasmon resonance (LSPhasave provided encouraging COVID-19 diagnosis capabilities [10]. The detection abilities were further enhanced through the generation of plasmonic heat on the same surface of AuNIs when they started to illuminate at their plasmonic resonance frequency. The locally generated PPT heat has the ability t increase *in situ* hybridization temperature which in turn enables differentiation of two same gene sequences. This dual functionalized LSPR biosensor has presented superb sensing performance in the detection of selective SARS-CoV-2 sequence with a low detection limit of 0.22 pM as well as allowed accurate determination of particular target in a multigene mixture.

Optical biosensors: First optical biosensor for commercial purpurposess introduced in the late 1980s, since then a large number of optical biosensors have been described in research and development, especially in the diagnostic and pharmaceutical industries. These researches include virology [11], epitope mapping [12], ligand fishing [13], cell biology [14], cell adhesion [15], bacteriology [16], nucleotide–nucleotide [17] binding, enzyme mechanisms [18,19], molecular engineering [20], nucleotide– protein [21,22], and signal transduction [23,24]. Optical biosensors offer some great advantages as compared to conventional analytical methods since they enable real-time, label-free, and direct detection of numerous chemical and biological substances. Their advantages include sensitivity, high specificity, cost-effectiveness, and small size [25]. Optical biosensors can develop cheap, multiplexed, and easily portable systems. Despite all these advantages, it can carry out label-free measurements. Newly fabricated nanostructures with sizes nanometers have the potential to direct light and can be utilized to examine different optical properties and phenomena of materials [26].

Glucose biosensors: The personal glucose meter (GM) is a typical device for point of care testing in household situations as of its comfort of use and consistent quantitative results. Recently, the DNA sensors, which were attached with a general GM were developed for the efficient detection of several targets, e.g., protein biomarkers [27,28] and recreational drugs [29,30]. Valentini et al. developed a glucose biosensor using gold microelectrodes coated via Single-Walled Carbon Nanotubes (SWCNTs), by the Electrophoresis Deposition Process. This nanostructured biosensor was successfully utilized to layer a poly (pyrrole)/glucose oxidase film. A highly extended linear concentration (ranging from 4 mM to 100 mM) of biosensor offered the opportunity to determine glucose levlevelsom 0.560 mM to 12.0 mM, with a high detection limit of 50 μM (useful for hypo-glycemia disease) [31]. A glucose biosensor working on the principle of direct transfer of an electron from glucose oxidase (GOD) and self-assembled over the surface of the electrochemically reduced carboxyl graphene (ERCGr) altered glassy carbon electrode has been prepared. X-ray photoelectron spectroscopy study of ERCGr showed that most of the oxygen-bearing groups in the carboxyl graphene, e.g., epoxy/ether and hydroxyl groups were removed excluding carboxylic acid. The cyclic voltammetric study of the electrode demonstrated a pair of quasi-reversible and well-defined redox peaks (-0.467 V) with a distance between peaks of 49mV, which revealed that the electron transfer has occurred in between the electrode and GOD. The

glucose biosensor exhibited a linear effect on the concentration of glucose in the range from 2 mM to 18 mM (detection limit=0.02 Mm) [32,33].

Dendrimer-Based Biosensors

Dendrimers are nanometer-scale 3D macromolecules in the size of an average protein-, and are hyper-branched, mono-dispersed, and star-shaped, with a high density of surface functional groups. The shape of dendrimers provides a vast surface area for the conjugation of biologically active molecules. They are composed of three distinct components: The core, the interior dendron, and the exterior surface with terminal functional groups [34,35]. They have been used extensively in various biosensors, diagnostics, and drug delivery based on electrochemistry, fluorescence, SERC, impedimentary, and SPR. Dendrimer based biosensors increase analytical sensitivity, stability, and reproducibility but reduce no specific interactions [36–37]. Bakar et al. detected dengue using a PAMAM dendrimer integrated tapered optical fiber sensor. The resolution and detection limit of the sensorwase 19.53 nM□1 and 1 pM, respectively, in the concentration range of 0.1 pM to 1 _M [38]. Fen et al. developed an SPR sensor based on self-assembled monolayer/reduced grapheme oxide-polyamidoamine dendrimer (SAM/NH2rGO/PAMAM) thin films to detect DENV-2 E-proteins. Their SPR sensor exhibited a detection limit of 0.08 pM DENV-2E-proteins in the range of 0.08 pM–0.5 pM [39].

Calorimetric biosensors: Calorimetric biosensors in the form of the enzyme thermistor and thermometric enzyme-linked immunosorbent assay (TELISA) have been extensively investigated by workers at the IJniversity of Lund and others over the past 15 years [40]. Early attempts to produce thermal enzyme probes (TEP) in which enzyme was immobilized directly on the thermistor were plagued by excessive loss of heat into the surrounding medium, resulting in insufficient sensitivity. The practical configuration adopted and exhaustively evaluted at Lund consists of an immobilized enzyme column housed in a temperature-controlled environment. The instrument is used in a flow-through mode and is intended for laboratory use, since it is relatively bulky. The present enzyme thermistor design does not match the market demand well. The vast majority of new markets for biosensors demand small, portable devices that are extremely easy to operate. There is naturally a continued requirement for more complex automated machines to handle large numbers of samples or for process control, but the competition from established, technology in this area is intense. Nevertheless, calorimetric approaches have one overriding attraction: they offer a single design concept that should be useful with virtually all biocatalysts. Recently there has been a notable revival in interest in both industrial and academic laboratories in the TEP. Advances in microfabrication technology have made more refined designs possible based on new, highly-sensitive temperature sensors. An integrated circuit calorimetric biosensor for glucose determination, which partially capitalizes on these advances, has been described by Muramatsu et aL. [41]

APPLICATIONS OF BIOSENSORS

Biosensors for Pathogen detection:

Different types of biosensor are being employed for detection of pathogenic microbes. It hels for the easy identification of the microbes present in body.[42]

Biosensors for cardiac biomarkers detection:

Many biosensors have been developed to detect a wide range of cardiac marker to reduce the costs for healthcare.[43]

Disease`s Cancer **diagnosis:**

Tumor development is linked with gene and protein changes generally come about because of the mutations and these changes can be used as biomarkers for the diagnosis. Cancer biomarkers are possibly a standout amongst the most significant tools for early cancer detection. Biosensors have been developed with an end goal to improve the analysis and treatment of different cancers. Aptamers, ssDNA, dsDNA, antibodies and typical antigens (p53 antigen) can be utilized as the bio-component in these biosensors.

Aptamer based on biosensors mutual with gold nanoparticles has been developed.

a. Alzheimer disease.
b. Diabetes mellitus.
c. Cardiovascular maladies.
d. Tuberculosis.
e. Hepatitis.
f. Diarrhoea.[44]

Biosensor for pharmaceutical

In the discipline of medical science, the applications of biosensors are growing rapidly. Glucose biosensors are widely used in clinical applications for the diagnosis of diabetes mellitus, which requires precise control over blood glucose levels.[45] Blood-glucose biosensors usage at home accounts for 85% of the gigantic world market.[46] Biosensors are being used pervasively in the medical field to diagnose infectious diseases. A promising biosensor technology for urinary tract infection (UTI) diagnosis along with pathogen identification and anti-microbial susceptibility is under study. Identifying end-stage heart failure patients, prone to adverse outcomes during the early phase of left ventricular assisted device implantation, is important. A novel biosensor, based on hafnium oxide (HfO2), has been used for early-stage detection of human interleukin (IL)-10.[47] Interaction between recombinant human IL-10 with corresponding monoclonal antibody is studied for early cytokine detection after device implantation. Fluorescence patterns and electromechanical impedance spectroscopy characterize the interaction between the antibody–antigen and bio-recognition of the protein is achieved by fluorescence pattern. Chen et al. applied HfO2 as a greatly sensitive bio-field-effect transistor.[48] HfO2 biosensor has been functionalized for antibody deposition with detec-tion of a human antigen by electrochemical impedance spectroscopy. The biggest dilemma faced today is of heart failure with about one million people suffering from it. Techniques for detection of cardiovascular diseases include immunoaffinity column assay, fluorometric, and enzyme-linkedimmunosorbent assay.[49–50] These are laborious, require qualified personnel and are time consuming. Biosensors established on electric measurement employ biochemical molecular recognition for desired selectivity with a particular biomarker of interest. The various other biosensors applications include: quantitative measurement of cardiac markers in undiluted serum, microfluidic impedance assay for controlling endothelin-induced cardiac hypertrophy, immunosensor array for clinical immunophenotyping of acute leukemias, effect of oxazabor- olidines on immobilized fructosyltransferase in dental dis-eases; histone deacylase (HDAC) inhibitor assay from resonance energy transfer, biochip for quick and accurate detection of multiple cancer markers and neurochemical detection by diamond microneedle electrodes

Biosensors and Cancer:

In terms of cancer, the analyte being detected by the biosensor is a tumor biomarker. Thus, by measuring levels of certain proteins expressed and/or secreted by tumor cells, biosensors can detect whether a tumor is present, whether it is benign or cancerous, and whether treatment has been effective in reducing or eliminating cancerous cells [51]. Biosensors that can detect multiple analytes may prove particularly useful in cancer diagnosis and monitoring, since most types of cancer involve multiple biomarkers [52]. The ability of a biosensor to test for multiple markers at once not only helps with diagnosis, but also saves time and financial resources [53]. A biosensor is made up of three components: a recognition element, a signal transducer, and a signal processor that relays and displays the results. The molecular recognition component detects a „signal‟ from the environment in the form of an analyte, and the transducer then converts the biological signal to an electrical output [54]

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