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Review Article

Biosensors: An Emerging Technology in Pharmaceutical Industry

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ABSTRACT

The evolution of biosensors has been the center of scientist's attraction for recent decades. It is a device which is used mainly for living organism or different biological molecules, enzymes or antibodies, to find out the presence of chemicals. Biosensors can basically serve as low-cost and highly efficient devices in addition to use in other day to day applications. Biosensor is a device that consists of two main parts: A bio-receptor and a transducer were as, Bio-receptor is a biological component that recognizes the target analytes and transducer is a physicochemical detector component that converts the recognition event into a measurable signal and quantify or it transforms one signal into another one, this works in a physiochemical way like Optical piezoelectric, electrochemical etc. Biomolecules like antibodies, enzymes, organelles, receptors and microorganisms as well as animal and plant cells or tissues have been used as biological sensing elements. In this paper, we review recent development and use of biosensors as a diagnostic tool, as well as some future applications of biosensor technology.

Keywords: Biosensors, Microbial biosensor, Transducer, Pathogen detection.

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INTRODUCTION:

Biosensors can be defined as, analytical devices consisting of a sensitive biological element and with a physical detector element it is also called transducer coupled to an input/ output device. [1] By the given definition, a biosensor is a self-contained integrated system, which detector determines an analyte of biological interest selectively and quantitatively with the help of bio-receptor element it also known as a bio-recognition element and a signal transduction element. [2] 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.[3]Biosensor is a device which combines with a biological recognition element with a physical or chemical transducer to detect a biological product. More technically, biosensor is a probe that combines with a biological one with an electronic component to yield a measurable signal as a product. [4]

Biosensors are currently enjoying an ever increasing use in a wide variety of applications and therefore are important that students and scientists in the analytical arena are aware of the range of biosensors that are available, the principals on which they are based and, most importantly, their advantages and limitations.[5] Biosensors represent

promising analytical tools applicable in numerous fields areas likein food industry, clinical diagnosis, environment monitoring and in other fields, where rapid and reliable analyses are needed. Some biosensors were successfully implemented in the commercial sphere, but majority needs to be developed in order to overcome the some imperfections.[6]

WHAT IS NEED FOR BIOSENSOR?

Sensitive and selective determination of various compounds of analytical and industrial relevance is one of the important and basic requirements of the present-day for the people working on it. Highly specialized instruments are being used for obtaining the desired information in the laboratories. Biosensors have the potential to measure constantly the presence/absence or concentration of specific organic or inorganic substances in desired specimens.

Bio-devices yield information rapidly and at reasonable cost. In this context, the increasing rate of obesity and the alarming rise in the rate of diabetes in the contemporary world is driving the need for easy-to-use devices to monitor diabetic patients' glucose levels. The pharmaceutical research industry urgently requires new rapid assay biosensors to speed the progress in drug discovery.[7]Some of the popular fields applying the use of biosensors in food industry to keep and check its quality and safety, to help

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distinguish between the natural and artificial; in the fermentation industry and in the saccharification process(The hydrolysis of polysaccharides to soluble sugars is called "saccharification".) to detect precise glucose concentrations; in metabolic engineering to enable in vivo monitoring of cellular metabolism.[8]

HISTORY OF BIOSENSOR:

The Father of the Biosensor is Leland C. Clark Jr. (1918–2005) was an American biochemist. He was born in Rochester, New York. He is most well known as the discoverer of the Clark electrode, a device generally used for measuring oxygen in blood, water and other liquids. Clark is considered as the "Father of Biosensors" and the modern-day glucose sensor used daily by millions of diabetics is based on his research. The history of glucose enzyme electrodes started in 1962 with the development and evolution of the first device by Clark and Lyons of the Cincinnati Children's Hospital. [9]

PRINCIPLE OF A BIOSENSOR:

Biosensor is a device that holds of two main parts: A bioreceptor and a transducer. Bioreceptor is a biological component that recognizes the mark analyte and transducer

is a physicochemical detector component that converts the recognition event into a measurable signal.[10]The desired biological material (normally a specific enzyme) is immobilized by conventional methods (physical or membrane entrapment, non- covalent or covalent binding). This biological material is in intimate direct contact with the transducer. The analyte binds to the biological material to form a bound analyte which in turn produces the electronic response that can be measured. In some instances, the analyte is further converted to a product which may be related with the release of gas (oxygen), heat, electrons or hydrogen ions. The transducer can convert the product linked changes into electrical signals which can be amplified and measured. Basically it is the investigation that mix a biological component with an electronic transducer thereby changing biochemical signals into electrochemical, optical, acoustic and electronic ones.[11]

DIFFERENT BIOSENSORS:

There are different biosensors which perform a variable role in the fields as provided. The following is a flowchart that represents different Classification of biosensors based on the transducer element & bio-recognition element.

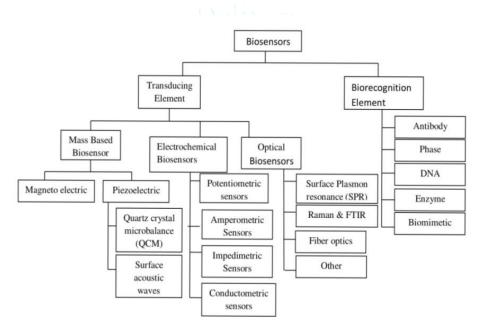


Fig -1: Classification of biosensors based on transducer element & bio-recognition element. [10]

BIOSENSORS WITH BIOLOGICAL EFFECT-BASED ANALYSIS:

Biosensors techniques utilizing enzymes, natural receptors, bacteria or cells can be used to rapidly identify toxicity and other biological effects in water containing different chemicals known as bio-sensing. The determination of toxicity furnishes an merged picture of the overall impact on the environment.

Research has been carried out where detection of arsenic is signaled as an easily detectable drop in pH and the chromogenic system. The endospores used can be stored and distributed in dried form without requiring freeze-drying or refrigeration. Whole organisms can also be used to measure the potential biological impact of a water or soil sample. Sensors for other areas of ecotoxicology, like genotoxicity and mutagenicity, has also been formulated, developed and described as "biosensors for environmental stresses". Genotoxicity is associated with different compounds, such as

phenols, chlorophenols, PCBs and PAHs, and can constitute an early warning screening parameter for possible cancer-inducing pollution activity. Mammalian cells, which are more complex than bacteria, can give a more sensitive response when compared to bacteria. In the particular case of pharmaceuticals, their environmental presence triggered a proposal to include an environmental risk assessment in the registration procedure for medical products. An ecotoxicological test battery has been designed for that [12]

TYPES OF BIOSENSORS:

The biosensors are of 5 types:

- 1. Calorimetric biosensors.
- 2. Potentiometric biosensors.
- 3. Acoustic wave biosensors.
- 4. Amperometric biosensors.
- 5. Optical biosensors.

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There are various types of biosensors based on the sensor devices and the some type of biological materials used. Electrochemical, amperometric, thermometric, optical, blood glucose, potentiometric, conduct metric, fiber optic lactate, optical for blood glucose, luminescent biosensors to discover urinary infections, piezoelectric, whole cell, and immune biosensors.[13]

1) CALORIMETRIC BIOSENSORS:

The use of calorimetry in bioanalysis has many attractive features, which were recognized early in studies by conventional calorimeters. Since biological reactions usually are more or less exothermic, calorimetry offers a general detection principle insensitive to the optical properties of the sample. Enzymic reactions are associated with rather high enthalpy changes in the range of 20-100 kJ mol-1 and it is often possible to base measurements on only one enzymic step in contrast to other techniques where the detection is based on, for instance, the change in concentration of colored reactants.[14]

Many enzymes catalyzed reaction are exothermic generating heat which is used as a basis for measurement of rate of reaction and hence analyte concentration. The temperature changes are determined by thermistors e.g. cholesterol biosensors using cholesterol oxidize (heat output 53 KJmol-1).[15]

2) POTENTIOMETRIC BIOSENSORS:

By combining a bio-recognition element Potentiometric biosensors are developed essentially an enzyme with a transducer that senses the variation in protons or other ions amount, the recorded analytical signal being logarithmically correlated with the analyte concentration.

It present Editorial deals with the presentation of several types of sensors based on different transducers and bio-recognition elements. Simplest transducer in the development of potentiometric biosensors is the glass pH electrode. Glucose oxidase immobilization achieved by using the cellophane, nylon or nitrocellulose membranes that are afterwards filed on the sensitive bulb of the pH electrode that senses the pH diminution, as a result of the bio-catalytical reaction occurring in the enzyme layer (glucose oxidation by glucose oxidase). This type of potentiometric enzyme sensors possess a linear range of 10-4 to $5\times10\text{-}2$ M, allowing for glucose assay in fruit injecs. [16]

3) ACOUSTIC WAVE -BASED BIOSENSORS:

Acoustic Wave –Based Biosensors are based on detection of mechanical acoustic waves and integrated a biological component. These are mass sensitive detectors, which are operated on the basis of an oscillating crystal that resonates at a fundamental frequency. After the crystals has been coated with biological reagents such as antibody and exposed to a particular antigen and quantifiable change occurs in the resonant frequency of the crystal, which is colligate to mass changes at the crystal surface. The huge majority of acoustic wave biosensors applies piezoelectric materials as the signal transducers.

Piezoelectric material is idea for use in this application due to their ability to generate and transmit acoustic waves in a frequency dependent manner. The physical dimensions and properties of the piezoelectric material influenced the optimal resonant frequency for the transmission of the acoustic wave. Generally most the commonly used piezoelectric materials include quartz (SiO2) and lithium niobate (LiTao3) which influenced the optimal resonant

frequency for the transmission of the acoustic wave. Emerging science, driving new sensors to deliver the molecular information that underpins all this, includes the development of semi synthetic ligands that can deliver the exquisite sensitivity and specificity of biological systems without the inherent instability and redundancy associated with natural molecules.

Currently aptamers, peptide arrays and molecularly imprinted polymers are particularly promising research directions in this respect. Chances of success are enhanced by the potential utility of some of these materials for novel therapeutic, antimicrobial and drug release strategies, since these complimentary areas will drive investment in these approaches.[17]

4) AMPEROMETRIC BIOSENSORS:

In amperometric approach, the signal transduction process is accomplished by controlling the potential of the working electrode usually an inert metal at a fixed value relative to a reference electrode usually silver chloride, and observing the current as a function of time. The applied potential serves as the driving force for the electron transfer reaction, and the current produced is a direct measure of the rate of electron transfer.

Amperometric biosensors take advantage of the fact that certain molecules can be oxidized or reduced at the working electrode i.e., gold, carbon, platinum, etc. If the working electrode is driven to a positive potential an oxidation reaction occurs, and the current flow depends on the concentration of the electro active species diffusing to the surface of the working electrode. Similarly, if the working electrode is impelled to a negative potential then a reduction reaction occurs. A third electrode called the counter or auxiliary electrode is often used to help measure the current flow. In most cases the bio-receptor molecule is immobilized on the working electrode, and as the analyte diffuses to the electrode surface the current generated reflects the retinae occurring between the bio-receptor molecule and analyte.

The amperometric sensor for glucose is the most studied of all biosensors, noting that it employs an enzyme (glucose oxidase) to catalyse the conversion of glucose to gluconic acid. Similarly, the amperometric approach has become widely used for the detection of nucleic acid and antigens for disease identification/diagnosis.In fact, amperometric transduction is the most suitable and common electrochemical detection method in immunosensors. These biosensors are highly sensitive, rapid and inexpensive. In addition, they display a high degree of reproducibility, which removes the need for repeated calibration. A possible limitation with amperometric transduction is the interferences that arise from electro active compounds/ species, and this can sometimes generate a false current reading. However, these problems have been largely eliminated by the use of electrodes coated with various polymers.[18]

5. OPTICAL BIOSENSORS:

Biosensors which signifies the end product of a quickly growing field, which combines fundamental biological, chemical, and physical sciences with engineering and computer science to satisfy needs in a broad range of application areas. Therefore, the term 'biosensor' has different connotations depending on what field the user comes from.[19]Causative agents of various infectious diseases are pathogenic microorganisms that are becoming increasingly serious worldwide. For the successful treatment of pathogenic infection, the fast and correct detection of

multiple pathogenic microorganisms is of huge importance in all areas related to health and safety. In the middle of various sensor systems, optical biosensors permit easy-to-use, rapid, portable, multiplexed, and cost-effective diagnosis. Here, we review current trends and advances in pathogen-diagnostic optical biosensors. [20]

OPTICAL BIOSENSORS FOR POLLUTION CONTROL AND EARLY-WARNING:

The increasing number of pollutants and their derivatives both in surface and ground waters as well as the stricter regulations for pollutant detection set by legislative bodies prompted great interest in a inexpensive general network system for pollution control and early warning. An early warning system (EWS) is an integrated system for monitoring, analyzing, interpreting, and communicating monitoring data, in which the continuous real-time detection is often performed using sensors/biosensors and a common warning or trigger an alarm is provided when a contaminant is detected in the water. The EWS identifies low probability/high-impact contamination events in sufficient time to safeguard public health.[21]

MAJOR CHALLENGE IN FRONT OF BIOSENSORS:

With all these diversified applications of biosensors, major challenges for biosensors is that out of hundred biosensors, only one is commercialized. Efforts of researchers can be seen in the form of advancements in the areas of biosensors. For commercialization, researcher's main focus is on low cost immobilization techniques. Research on these new immobilization materials is unstoppable as new materials are experimented daily in laboratories to get new best one. Secondly, to decrease and increase precision and accuracy to advertise biosensor in market, nanostructures like nanowires, nanorods and nanotubes are utilized in electrochemical biosensors. Carbon nanotubes (CNTs) is not only raise stability of immobilized biomolecules, rather, in addition, enhances sensitivity of biosensor. Besides, these CNTs can be used to fabricate electrodes which offer advantage of rise in electron transfer, reproducibility and stability of biosensor .To state the matter differently, CNTs can be used as amplifiers in biosensors. Apart from these Carbon nanotubes i.e CNTs, other materials like porous silicon also are of great importance as substrate/support in biosensors. Now a days other flexible particles which are in focus are magnetic nanoparticles. Moreover, due to the fact of high sensitivity and specificity of nanostuctures, they have been used to sense various analytes like hydrogen peroxide, glucose, cholesterol, DNA, inosine, bacteria, cancer etc. For further efficiency of biosensors, graphene entered into the field of biosensors due to its more surface area and electrical conductivity.

Various graphene based electrochemical biosensors, to detect concentration of heavy ions in environment, have been develop. In medical and forensic science, grapheme based on electrochemical DNA biosensors has been developed to detect genetic disorders and criminals. In addition to commercialization, researchers are concentrating on other aspects of biosensors; it is to make multiple analyte detecting integrated biosensors in every possible field and implantable biosensors in medical field.[22]

APPLICATIONS OF BIOSENSORS:

1. Biosensors in Medical Diagnostics medium:

Medical Diagnostics represents has a huge well-established demanded market of biosensors. With increasing level of health problems, there increasing demand for inventing rapid and sensitive as well as modern methods of diagnostic devices.

2. Biosensors in Food and Agriculture level:

As we know that India is a growing Nation, and agriculture is the basic prime source of income. The increasing consumer demands for quality and safe food requires a lot of efforts for quality control by the industries.[23]

3. Biosensors and 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. [24]

4. Environmental Monitoring:

Pollutants in the environment are great risks for the health of human beings. Several microbial biosensors are used for detection of organic and inorganic toxicities being extensively used in industry, heavy metal become a main toxicant in waste water.

5. Food and Fermentation:

Recent developed microbial biosensors used in food and fermentation. Fermentation is widely used for the production of foodstuffs and drinks, which requires a carefully performed fermentation system operation. Microbial biosensors are used to monitor the materials in order to control the fermentation process.[25]

6. Biosensors for cardiac biomarkers detection:

Many biosensors have been developed to detect a wide range of cardiac marker to reduce the costs for healthcare. [26]

7. Disease Diagnosis.

8. 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.[27]

9. Biosensors: Industrial Biotechnology:

Biosensors and Food had borne Bacteria Monitoring.

Milk Purification, The market trends showed about 10.4% growth in the development of biosensors for various applications, like in biopharma, food and beverages, biodefense, and environmental analysis. Biosensor devices are ideal tools for environmental monitoring because they are sensitive, selective, easy, and rapid.

Novel electrochemical biosensor was constructed for determination of cholesterol levels by Satvekar and coauthors. Bioenzymatic nanobiosensor was based on DNA-assembled Fe3O4Ag nanorod in silica matrix entrapping enzymes cholesterol oxidase and horseradish

peroxidase onto surface of indium tin oxide electrode. Cholesterol levels were determined by cyclic voltammetry with limit of detection 5.0 mg/dl and linear range between 5.0 and 195 mg/dl.[28]

FUTURE PROSPECTIVE AND CHALLENGES:

Biosensors have extensive prospective applications in these different domains as screening and monitoring of both public as well as personal health, pathology, environmental monitoring e.g. the detection of pesticides, river water contaminants, etc., bioprocess, criminology, civil defense, and within the industry of food, water quality and beverage for safety. [29] Biosensors are widely used in biomedical research, health care, pharmaceuticals research via spatially separated molecular probes immobilized on a solid surface to scrutinize or detect biomarker for diagnosis of various diseases.

Fortunately, the development of biotechnology, nanotechnology and novel immobilization strategy in the past years the nanobiosensors are becoming more powerful in the field of medicine.[30] The future prospects of whole cell-based biosensors may prove exciting. An early example of what this future might hold was demonstrated in a report on a portable whole cell-based optical biosensor named Luisens 2 developed to provide real-time online detection of pollutants.[31]

CONCLUSION:

Biosensors have been miniaturized extensively in the recent years. Keeping in line with such developments, microbial cells with high enzyme behaviors may be needed. This is main and definitely when microbial cells are applied as replacements to enzyme based sensors. Due to the low cost of microorganism, long lifetime and broad range of suitable PH and temperature, have been widely employed as the biosencing element in the construction of biosensors. So the proper use of biosensors should be done in order to have a great benefit in future.

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