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REVIEW ARTICLE
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Biosensors: tool for food borne pathogen detection

Heena Sharma[1], Megha Agarwal[2], Meena Goswami[3], Anupama Sharma[4], Sanjeev K. Roy[1], Rinita Rai[5] and M.S.Murugan[6]

1. Division of Livestock Products Technology, Indian Veterinary Research Institute, Bareilly-243122, Uttar Pradesh, India; 2. Division of Animal Biotechnology, Indian Veterinary Research Institute, Bareilly-243122, Uttar Pradesh, India; 3. Division of Livestock Products Technology, DUVASU, Mathura-281001, Uttar Pradesh, India; 4. School of Public Health and Zoonoses, GADVASU, Ludhiana- 141001, Punjab, India; 5. Division of Bacteriology & Mycology, Indian Veterinary Research Institute, Bareilly-243122, U.P, India; 6. Avian Diseases Laboratory, Thalaivasal-636112, Tamil Nadu, India
Corresponding author: Heena Sharma, email: heena_vet@yahoo.com
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Abstract

A paramount and alluring sphere of research, now-a-days, is food analysis, because of the breakneck augmentation of food enterprise and highly hightened maneuverability of today's populations. The management of food quality is very indispensable both for consumer safeguard as well as the food corporations. The biosensors' application in the field of food analysis is quite propitious for the revealing of food borne pathogens. Biosensor, an analytical device, transforms a biological response into an electrical signal. Bioreceptors and transducers are the two main components of a biosensor. Bioreceptor or biorecognition element is the one which leads to the recognition of target analyte and a transducer, for the conversion of recognized event into a measurable electrical signal. The development of biosensors improved the sensitivity and selectivity of detection techniques for food borne pathogens and is rapid, reliable, effective and highly suitable when used in *in situ* analysis. Since the security in the food supply becomes crucial because of increased perception among consumers and vying nature of food industries, the necessity for expeditious, low volume and sensitive biosensor devices has productively increased. Nevertheless , till date, a very few biosensor systems are available commercially such as Biacore, Spreeta™, Reichert SR 7000, Analyte 2000, RAPTOR etc. Since, there is ever growing concern regarding safe food and water supply, it is very obvious that the demand for rapid detecting biosensors will also be increasing at par.

Keywords: bioreceptor, biosensors, food borne pathogen, transducer

Introduction

Food products and their raw materials are composed of complex compounds, therefore, to guarantee its high-quality principles and security, the quality control is the foremost task allied with food industries [1]. Even if the food security has significantly enhanced , advancement is uneven, furthermore microbial contamination, chemicals and toxins leading to food borne outbreaks are widespread in several countries. It has been estimated that the food industry spends on an average, 1.5%-2% of the value of its total sales on quality control and appraisal [2]. According to a new market report of Strategic Consulting Inc. entitled Food Micro 2005, the worldwide food microbiology market in 2005 represented over 25 million $ tests with a market value in excess of 1.65 billion $ [3]. Food manufactured might be microbiologically contaminated at base level or at either stage while processing, packaging or distribution. Biosensors have elevated potential for automation and permit the construction of simple and portable equipment for fast analysis [4]. For the reason that most food is extremely sensitive to critical process parameters and can effortlessly undergo rapid and destructive changes, process control is chief point in a modern industrial environment. Hence, there is an expanding demand for analytical technology appropriate for automatic quality control through the process and at the end of the line so that the real-time state of the process can be restricted [5]. In addition to rapid results, on-line biosensor technology offers food industry a choice of internal process control to fulfill the interest of a high standard of quality control.

Biosensor is an analytical device assimilating a meticulous and essential amalgam of a specific biological element (that constitute a perceptive action) and a physical element (that transduces the perceptive action). For easy understanding, the term biosensor signifies a fusion of biology and sensing, a sensor competent enough to recognize an analyte, a biological sample, and transmit and interpret signal [6]. The finest illustration of a biosensor in human body is the nose, competent of distinguishing odor molecules and transmitting a signal to the brain. It comprises of two chief components: a bioreceptor or biorecognition element, which perceives the desired analyte and a transducer, for translating the predicted event into a quantifiable electrical signal [7]. The fundamental characteristics of a biosensor [8] comprise linearity (linearity of the sensor should be high for the detection of high substrate concentration), sensitivity (Value of

Table-1. Classification of biosensors

Classification of Biosensors			
Mechanism of biological selectivity		**Mode of physiochemical signal transduction**	
Biological selectivity	**Biological component**	**Principle**	**Transducer**
a) Bioaffinity	Antibody-antigen,Oligonuceotides	a) Electrochemical	Amperometric, Potentiometric, Impedimetric
b) Biocatalytic	Enzymes	b) Optical	SPR
c) Micro-organism Based	Whole cells	c) Acoustic	Piezoelectric (Mass sensitive)

the electrode response per substrate concentration), selectivity (chemicals interference must be minimized for obtaining the correct result) and response time (time necessary for having 95% of the response).

The first biosensor was characterized by Clark and Lyons in 1962. A Clark oxygen electrode was combined with the enzyme glucose oxidase to monitor glucose levels. The co-reactant oxygen could be monitored amperometrically which was produced while glucose underwent enzymatic oxidation [9]. On the other hand, the production of hydrogen peroxide during the enzyme reaction could be measured. Since then, much work was published on enzyme electrodes. Enzymes were immobilized with diverse procedures and reaction substrates or products were revealed by distinct methods. In 1969, Guilbault and Montalvo reported the first enzyme biosensor based on potentiometry. Rchenitz charcterized a selective NH_3 gas sensing electrode for arginine in 1977 and used the term 'bioselective sensor' and this term was at a later date abbreviated to “biosensor” [10].

Classification of biosensors

Conventionally biosensors may be classified (Table-1) according to the mechanism of biological selectivity (bioreceptor) otherwise, on the mode of physiochemical signal transduction (transducers).

Bioreceptors: A bioreceptor is a molecular species that exploits a biochemical mechanism for recognition. They are accountable for binding the concerned analyte to the sensor for measurement [7]. Bioreceptors can broadly be classified into five distinct classes. These classes comprise antibody-antigen bioreceptor, enzymatic bioreceptor, nucleic acids (DNA) bioreceptor, cellular structures or cellular bioreceptor, biomimetic bioreceptor and bacteriophage bioreceptor.

Antibody bioreceptor: Antibodies are universal bio-receptors used in biosensors. The antibodies may be polyclonal, monoclonal or recombinant based on their selective properties and synthesis. Nonetheless, they are usually immobilized on a substrate, which can be the detector surface, its vicinity, or a carrier [11]. An antigen-specific antibody fits its exclusive antigen in extremely specific way alike to a lock and key [12], so that the three-dimensional structures of antigen and antibody molecules are corresponding. This inimitable property of antibodies is the key that makes the immunosensors influential analytical tool and their skill to distinguish molecular structures allows one to develop antibodies that bind exclusively to any of the chemicals or biomolecules or microorganisms etc.

Enzyme bioreceptor: Enzyme as bioreceptors offer numerous advantages over fluorescently labeled and radio labeled substances and enzyme immunoassay reagents are highly stable, sensitive and there are no health hazards. Enzyme immobilization emerges as a fundamental aspect to evolve competent biosensors with relevant properties such as good operational and storage stability, immense sensitivity, high selectivity, short response time and large reproducibility [13]. The most frequently used enzyme is Horseradish Peroxidase (HRP) and beta-galactoxidase. The detection of pathogenic bacteria such as *Listeria monocytogenes*, *Escherichia coli* and *Campylobacter jejuni* can be done by labeling the antibody with these enzymes.

Bacteriophage bioreceptors: Bacteriophages (phages) are viruses of 20-200 nm in size [14] that unite to definite receptors on the bacterial surface in order to infuse their genetic material inside the bacteria. Phages identify the bacterial receptors via its tail spike proteins. They have noticeable edge over other biorecognition receptors. Amid these, advantages are the specificity of the synergy of this sort of virus with its target host cell, its skill to lyse and kill its host, plus its ability to reproduce throughout the infection process [15]. In addition, they are omnipresent, innocuous to humans, economically and conveniently produced, have a distant longer shelf life as they endure harsh environments, diminishing the environmental limitations and enabling regeneration of the biosensor surface. Researchers have proclaimed the function of phage as a biorecognition component for the exposure of various pathogens such as *E. coli* [14], *Staphylococcus aureus* [16] and *Bacillus anthracis* spores [17,18] by adopting diverse sensing platforms.

Nucleic acid bioreceptors: The precise biorecognition in DNA biosensors depends on the complementarity of adenine: thymine (A:T) and cytosine:guanosine (C:G) pairing in DNA which is known to form the foundation for, generally referred to as genosensors. Nucleic acid based biosensors have been proclaimed by several researchers for the detection of food pathogen like *E. coli* O157:H7 [19], *Salmonella spp.* [20], *C. jejuni* [21] etc. An additional type of biosensor employs a peptide nucleic acid as the biorecognition element [22]. The peptide nucleic acid (PNA) is a synthetic oligo amide that is competent of binding incredibly firmly to complimentary oligonucleotide sequences. Although the major drawback of PNA is that their synthesis is very costly. But the key disadvantage is that Purine-rich PNA oligomers tend to cumulate and are weakly soluble in aqueous media [23].

Cell based biosensor: Cellular structures and cells have been operated in the evolution of biosensors and biochips [24]. Isolation of cell organelles can be done for utilizing them as bioreceptors. Cell organelles are necessarily exclusive system which recognizes it to be exploited for long course of time. Mammalian tissue slices or *in vitro* cultured mammalian cells can be well employed as biosensing elements in bioreceptors [25]. The reason for suitability of living cells as recognition element are [7] :a) they provide sensitivity to biochemical stimuli, secondly, b) they present functional analysis for biochemical agents and lastly, c) their detection can be very low due to signal amplification. The elementary illustration of a cell-based sensing system using collagen-encapsulated mammalian cells for rapid detection of pathogenic bacteria or toxin was presented by Banerjee et al. [26]. Advancement of an artificial cell-based biosensor, which exploits liposome-doped silica nano-composite, has been noted by Zhao et al. [27]. It mimics existing whole-cell assays for Listeriolysin O (LLO) which is a pore-forming hemolysin secreted by pathogen *L. monocytogenes*.

Transducers: The transducer plays a crucial part in the detection and identification process of a biosensor. Biosensors can also be designated on the basis of the transduction systems they engage. The transduction methods such as optical, electrochemical and mass based are the most favored and universal methods.

Mass sensitive biosensors: Assessment of minute transformation in mass is a distinct configuration of transduction that has been exploited for biosensors. The fundamental mode of mass analysis relies on the account of piezoelectric crystals [28]. This results in the vibration of crystals at a distinct frequency with the operation of an electrical signal of explicit frequency. Therefore, the frequency of oscillation depends on the electrical frequency which is applied to the crystal and its mass [7]. Thus, in simple words, binding of chemicals results in increase in mass which in turn changes the oscillation frequency of the crystal which can be measured electrically and utilized in the determination of the additional crystal mass. The detection of *L. monocytogenes* has been conceivable with the development of a quartz crystal microbalance biosensor [16].

Electrochemical biosensors: These are addendum of conventional antibody based enzyme immunoassays (ELISA), which comprises the catalysis of substrates by an enzyme conjugated to an antibody and the production of products which in turn can be detected in the pattern of pH change, ion or oxygen consumption due to generation of electrical signals on a transducer [7].

Amperometric biosensors: Amperometric transduction is universal electrochemical detection method which has been well exploited for pathogen detection. This technique is very integral to optical detection methods such as fluorescence, which is considered as the most precise of the optical techniques [29]. These sensitive biosensors can also be used in order to identify various food borne pathogens viz., *E. coli* O157:H7 [16], *Salmonella* [30], *L. monocytogenes* [31] and *C. jejuni* [32]. The scope of electrochemical biosensor has developed expeditiously in eventual few years. There has been immense breakthrough in the advancement of electrochemical sensors for detecting virus infection and bacterial contamination [7]. Reymond et al. [33] devised an amperometric detection method for the determination of the presence, the amount, and the concentration of an analyte in a micro fluidic sensor. There have also been disclosures related to the evolution of a biosensor for the estimation of protein and amino acid [34]. Electrochemical biosensors developed on the basis of amperometric detection were found linked with other biosensing techniques. For example, a bienzyme electrochemical biosensor was found helpful in the detection of pathogens like *E. coli* O157:H7 [35], *Salmonella* Typhimurium [36].

Potentiometric biosensors: Potentiometric biosensors involve the utilization of ion-selective electrodes in order to transduce the biological reaction into an electrical signal. Thus, it is simply comprised of an immobilised enzyme membrane which surrounds the probe from a pH-meter and the hydrogen ions are generated or absorbed here via catalyzed reaction. The reaction happening adjunct to the thin sensing glass membrane directs the change in pH which can be read directly from the pH-meter's display. Light-addressable potentiometric sensor (LAPS) for the detection of pathogens has been reported [37]. Gehring et al. [38] developed an immune-ligand assay (ILA) in conjunction with a light-addressable potentiometric sensor (LAPS) for the rapid detection of *E. coli* O157:H7 cells in buffered saline. Zhang et al. [39] has developed a potentiometric flow biosensor based on ammonia-oxidizing bacteria for the detection of toxicity in water.

Impedimetric detection: The thought of electrical impedance measurement of microbial growth was put forward by G.N.Stewart in 1899, however, the method was employed for the first time in 1970s for this purpose. Impedance is defined as the apparent resistance in an electric circuit to the flow of alternating current, which corresponds to the actual electrical resistance to a direct current. Thus, its principle is based on the changes in the conductance of the medium due to microbial metabolism of the inert substrates into electrically charged ionic compounds and acidic-by-products (e.g. amino acids, lactic acid and acetic acid).This causes a change in electrical impedance and conductance of the medium. Bacterial growth in a medium which can be related to the function of time at a given temperature can be monitored by carefully monitoring and measuring electrical impedance and conductance.

At present, impedance instruments are able to detect 10^5-10^6 bacteria/ml. Some commercially available

Table-2. Commercially available biosensors (The names of commercial products/companies used in this study are for information purpose only. Authors or institute of authors do not recommend the use of these products)

Manufacturer	Instruments	Target compounds	Food sample
Biacore AB	Biacore Q	Folic acid, Biotin, Antibiotics	Cereals, meat, milk, Infant food, Honey
Texas Instruments Inc.	Spreeta™	Ingredients, Contaminations	Beverages
Research International Ltd.	Analyte 2000™	*E. coli* O157:H7	Hamburger
Malthus InstrumentsLtd.	Malthus systems	*E. coli* O157:H7, Fungi, Yeast	Shell fish
Don Whitley Scientific Ltd.	RABIT	Food pathogens	Vegetables
Innovative Biosensors Inc.	Bioflash™ system	*E. coli* O157:H7	Lettuce

Table-3. Upcoming biosensors in near future (The names of commercial products/companies used in this study are for information purpose only. Authors or institute of authors do not recommend the use of these products)

Company	Development	Aim
Axela Biosensors, Inc.	DOT™ sensor and DOT™ reader	Applications in agricultural, environmental and food & beverage sector
Biophage Pharma Inc.	Phage Biosensor	*E.coli* O157:H7, *Campylobacter*, *Salmonella* in water
Universal Sensors, Ltd.	UTS™ technology	Aqueous-based samples
AKUBIO Ltd.	RAP id™ 4	Resonant Acoustic Profiling technology for molecule interaction in complex matrices
Stratophase, Ltd.	Refractive Index sensor chips	Liquid Samples

systems such as the Bactometer (bioMerieux), Malthus AT analyzer (Malthus Instruments), BacTrac™ are used for pathogen monitoring and quality assurance purposes. Yang et al. [40] used inter-digitated micro-electrodes as impedance sensors for rapid detection of viable salmonella.

Optical biosensors: Optical biosensors are dynamic substitute to accustomed scientific techniques which can be well related to their particularly high specification, sensitivity, small size, and relatively cost effectiveness [41]. The research and high-tech development of optical biosensors have gained an exponential growth during the last decade because of the linear, real-time and label-free detection of many chemical and biological substances by this technique [42].

Raman and Fourier Transformed Infra-red Spectroscopy (FT-IR): Fourier transform spectroscopy is a computational technique which involves the collection of spectra based on calculation and evaluation of the coherence of a radiative source with the help of time domain or space-domain measurements of the electromagnetic radiation or any other type of radiation. Schmilovitch et al. [43] operated a dispersive system spectrophotometer, with a 785 nm diode laser for the detection of Gram-positive and Gram-negative bacteria. Whereas, another application of this technique includes the detection and differentiation of live and heated *Salmonella enterica* serovars inoculated onto chicken breast by Davis et al. [44]. FT-IR has also been exploited for the compliation or recognition of various food borne pathogens: *Yersinia, Staphylococcus, Listeria, Klebsiella, Enterobacter, Citrobacter, Salmonella*. FT-IR spectrometry can be implemented to detect *E. coli* O157: H7 from ground beef [45].

Surface plasmon resonance (SPR): SPR is a robust tool that can measure the binding kinetics of two molecules without the help of any fluorescent tag. Thus, this technique can be said as a peculiarity that appears during optical illumination of a metal surface and can be adopted for biomolecular interaction analysis. The advantages affiliated with this are that it takes less time to detect binding events and since it is label-free, it excludes additional reagents, assays and steps. There have been many reports on SPR based biosensors by various researchers for the identification of different food borne pathogens such as *L. monocytogenes* [46], *Staphyloccocus* [47], and *E. coli* O157:H7 [48,49]. Commercially available SPR systems are also available now which includes: BIACORE, Spreeta™ , SPR spectroscope, Optrel GbR, Reichert SR7000 and IAsys. Among all these, the detection of *E. coli* O157:H7 [50] and *L. monocytogenes* [51], *Salmonella* [52] can be done by Spreeta™ biosensor and BIACORE 3000 respectively.

Commercially available biosensors

Regardless of the enormous collection of publications on biosensors implemented in food analysis, there are very limited entities which are commercially available [53]. The utilization and commercialization of biosensor technology has diminished far behind the output of research laboratories. There are many biosensor-related patents filed each year, however very few play a prominent role in food industry (Table-2). There have been many apprehensions for the slow technology transfer from the research laboratory to the market place: limited lifetime of the biological components, mass production, quality assurance and instrumentation design and the most decisive one is the lack of cogency, organized commercialization approaches.

Upcoming techniques, future developments

The most promising breakthroughs are to be expected in the area of biosensor technology (Table-3), that will allow the creation of on-line or on-site, sensitive, low-cost devices for routine use [53]. Biosensors have high potential for automation and allow the construction of simple and portable equipment for fast analysis. Biosensor advancement, in the commercial world could be accelerated by the use of intelligent instrumentation, electronics, and multi-variate signal-processing methods.

Conclusion

Food has a far-reaching aspect in aggrandizing, and invigorating health and quality of life. To comply with consumer desideratum and cater healthy and high-quality food, the production and processing distribution chain has to be meticulously checked. There is a huge requisite for expeditive and nominal techniques to clinch quality of products and process control in the food industry. The pertinence of biosensor techniques in the field of processing and quality supervision endeavor advantages alternatives to conventional methods due to briskness, cost efficiency, high sensitivity, and specificity of assessments. The promise shown by biosensor technology is very promising but still there are technological problems to be deciphered. Additionally, the market penetration has to be improved for areas where biosensor technologies are quintessential for elevating food diagnostics. As interests about safe food and water supply augment, the demand for swift recognized biosensors will also boost up.

Competing interests

The authors declare that they have no competing interests.

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