

# The Use of Biosensors for the Detection of Chemical and Biological Weapons

[Kimyasal ve Biyolojik Silahların Saptanmasında Biyosensörlerin Kullanımı]

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## ABSTRACT

A wide spectrum of chemicals, toxins and microbiological materials including some bacterial exotoxins has potential for use in a warfare or terror attacks. Both civilian and military sources predict that over the next decade the threat from proliferation of these chemical and biological warfare agents will increase significantly. Recent terrorist events and threats have shown that an urgent and effective method is required for sensing the threat detection, especially chemical and biological warfare agents. So, reliable and rapid detection and identification of these biochemical agents is one of the primary concerns that physicians and other health staff have to deal with. In this paper, biosensor, which is one of these prominent detection systems is overviewed from the aspect of medical response against these weapons. Application fields of biosensors highlighting the use in detection and identification of biochemical weapons of mass destruction have been described to emphasize the trends on new technology of sensors. Various types of sensors have been developed and extensively evaluated on field. This paper also describes this developing technology for detecting such agents. It may be envisaged that national capability to detect these terror agents rapidly should be improved in terms of recognition of the exposure.

**Key Words:** biosensor, chemical, biological, weapons, detection.

## ÖZET

Geniş bir spektrumda kimyasalların, toksinlerin ve bazı bakteriyel ekzotoksinlerin de dahil olmak üzere mikrobiyolojik materyallerin bir savaş veya bir terör ortamında kullanıma potansiyeli bulunmaktadır. Hem sivil hem de askeri kaynaklar önmüzdeki dönemlerde bu kimyasal ve biyolojik savaş ajanlarından doğabilecek tehdidin artabileceğini tahmin etmektedirler. Son terör olayları ve tehdidi de göstermektedir ki, bu kimyasal ve biyolojik ajanlardan kaynaklanabilecek bu tehditlerin ortaya çıkarılması için acil ve etkili bir yönteme ihtiyaç bulunmaktadır. Bu biyokimyasal ajanların güvenilir ve süratli bir şekilde saptanması ve tanınması hekimlerin ve diğer sağlık personelinin üstesinden gelmesi gereken konulardan birisidir. Bu makalede, önde gelen saptama sistemlerden olan biyosensörler, bu ajanlara karşı verilecek tıbbi yanıt açısından gözden geçirilmektedir. Biyokimyasal kitle imha silahlarının saptanması ve tanınmasında uygulanmasının öne çıkarıldığı biyosensörlerin kullanım alanları yeni sensör teknolojileri vurgulanarak anlatılmaktadır. Çeşitli tipte sensörler geliştirilmiş ve geniş bir şekilde alanda denenmiştir. Bu makale bu ajanların saptanması için bu gelişmekte olan teknolojiden de bahsetmektedir. Maruziyetin ortaya konulmasında bu terror ajanlarının süratle saptanması için ulusal yeteneklerimizin geliştirilmesinin de gerekli olduğu öngörülmektedir.

**Anahtar Kelimeler:** biyosensör, kimyasal, biyolojik, silah, saptama

## Overview on Biosensors

Biosensor is an analytical device with a biological element, which transforms chemical parameters within a system into an optical or electrical signal (1).

Thus, a biosensor consists of a bioreceptor and a transducer. Bioreceptor is a biomolecule, which can identify the analyte targeted to be found out, but transducer is a component, which transforms the identified value into a signal that can be measured. These two components are integrated into a system to form a biosensor.

**Table-1:** The application fields of biosensors are wide as is mentioned below

<ul style="list-style-type: none"><li>- Clinical diagnosis and biomedicine</li><li>- In agriculture field and veterinary applications</li><li>- Fermentation control and analysis of the food and drink production</li><li>- Microbiology, bacterial and viral analysis</li><li>- In pharmaceutical field and medicine analysis</li><li>- Control of the industrial waste</li><li>- Control and monitoring of environmental pollutants</li><li>- Military applications</li></ul>
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Use of biosensors in identification of chemical and biological warfare agents:

Chemical and biological warfare is to cause disease of human beings and animals or to use chemicals and biological agents to damage foods or materials and plants. One of the important ways of the protection against such toxic agents is to ensure early diagnosis and therapy, effective intelligence, and improvement and use of information technology. Currently, conventional methods are still used to detect these chem-bio agents. However, the information about which microorganism or which agent is used during an attack before causing the disease or exposure, will allow us to early diagnose the possible disease and apply an effective and appropriate treatment and approaches against it. Therefore, such biosensors, which can allow rapid and precious diagnosis, have been designed in recent years in particular. It is obvious that there is an increasing need for rapid and cost-effective commercial devices to detect microbial contamination of food, industrial water wastes and clinical samples. This caused the development of biosensors in recent times in order to ensure microbial detection of microorganisms and chemical terror materials based on their optical, electrochemical, biochemical and physical features (2).

Sometimes a whole cell can also serve as a bioreceptor. Microbial cells immobilized on electrodes are used as detectors. Here, the oxygen consumption is measured based on the microbial metabolism. Microorganisms are immobilized on a cellulose membrane and this complex is integrated into a membrane, a reacting layer, to set up

a system. In this system, *Rhodococcus erythropolis* and *Issatchenkia orientalis* may be used as the basic microorganisms (2).

In addition, the Man-portable Analyte Identification System (MANTIS) has been developed. This system is a fiber optic biosensor that is used for detecting the staphylococcal enterotoxin B, a bacterial toxin of *S. aureus*, which mostly causes food poisoning. This system can be used in the field and identify the toxin in liquid and gas samples (3).

New Horizons Diagnostics Corp. (NHD) has also developed a sensor by using modified larger colloidal gold particles within a small plastic cassette and recombinant FAB antibodies. According to this system, it is possible to detect 3 nanograms of botulinum toxin positivity within 5 minutes (4). Another system developed by the same company allows the identification of live bacteria in the air or liquid by determining ATP contents of the bacteria within a time less than 1 minute. In this system, the sample is mixed with BRA (Bacterial Releasing Agent), this mixture is transferred to a membrane covered with luciferin-luciferase and the emission of light correlated with existing ATP is measured by an illuminometer (5). In addition, a biosensor is reported to be developed against staphylococcal enterotoxin B (SEB) that has the potential to be used as a biological weapon. Here, a 20-MHz piezoelectric quartz crystal sensor has been integrated into a flow-injection system and polygonal antibody is used where detection limit is 0.1- µg/ml (6).

Similarly, Frances Ligler and his colleagues from George Town University Naval Research Laboratory have developed a sensor able to identify the bacteria in the air. This fiber-optic system based on Antigen-Antibody reaction performs the sampling by remote controlling on the ground and identifies the agent and transmits the resulting data to the operator. The antibody that is developed against the fluorescence-marked is immobilized on the fiber on which the avidin-biotin molecules are cross-linked. In this system, the detection limit is 3000 colony/ml and the air volume it can sample is 100 L/min (7).

Furthermore, efforts have been spent to use the biosensor technology to ensure early detection of chemical warfare agents, especially nerve gases. The fact that nerve gas agents have the same structure with organophosphorus insecticides has facilitated these studies (8,9).

It is also possible to express acetylcholinesterases in vitro and use as a biosensor for detecting organophosphates and carbamate insecticides (10). For this purpose, enzyme expression has been made from bovine erythrocyte, *Electrophorus electricus*, *Drosophila melanogaster*, *Torpedo californica* and *Caenorhabditis elegance*. As a result, it has been found out that *D. melanogaster* is 8 times more sensitive to the enzyme than *E. electricus*, and this sensitivity may increase up to 12 times due to a mutation in 408<sup>th</sup> position. (11)

Similarly, a biosensor has been developed based on the method of potentiometric enzyme electrode to provide

direct measurement of organophosphorus nerve agents. In this system, organophosphorus hydrolase is immobilized via cross-links with bovine serum albumin and glutaraldehyde and bound to a pH-electrode. It is based on the measurement of the amount of protons resulting from the hydrolysis of the enzyme in proportion to the concentration of enzyme substrate. The best sensitivity and response time in this method has been achieved by the sensor operating in 1- mM HEPES buffer, 8.5 pH, which has been developed with 500 IU organophosphorus hydrolase. Similarly, it has been found that such organophosphoric compounds including 2  $\mu$ M paraoxon, ethyl parathion, methyl parathion and diazinon have been measured under same conditions (12).

In addition, for detecting OP nerve agents, a fiber-optic microbial biosensor has been developed by using recombinant *E.coli* cells. It is based on the detection of end products obtained as the result of organophosphorus hydrolysis catalyzed by OP hydrolase expressed in the cell surface. It has been pointed out that this system is advantageous in comparison to traditional microbial sensors and enzyme-based sensors because of the fact that such cells containing metabolic enzymes on the surfaces are used, and analytes and products do not show any resistance during the transition through cell membrane, and it is cost effective due to the elimination of the enzyme purification (13).

Additionally, in another biosensor developed, OP pesticides and recombinant *E.coli* cells have been used to directly identify OP neurotoxins and to hydrolyze chemical warfare agents having this structure. Here, a potentiometric system has been used as transducer (13).

## Conclusion

The biosensors to be used in the detection of WMD including biological and chemical weapons must have a high sensitivity and their sensitivities must be increased to nanomole, even picomole levels. In our country facing the potential threat of biological or chemical attack, related studies must immediately be accelerated with multidisciplinary efforts and a biosensor network must be developed to detect such an attack in a short time and take the required measures.

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