CHAPTER: 09

EMERGING TREND OF BIOSENSORS IN DIAGNOSIS OF URINARY TRACT INFECTION

[1]TANUSHRI CHATTERJI

[1]Assistant Professor, School of Bioscience, IMS Ghaziabad (University Courses Campus), Adhyatmik Nagar, NH-09, Uttar Pradesh, Ghaziabad

[2]NAMRATA KHANNA

[2]Senior Lecturer, Department of Biochemistry, Babu Banarasi Das College of Dental Sciences, Babu Banarasi Das University, Faizabad Rd, Atif Vihar. Uttar Pradesh, Lucknow

[3]SURUCHI SINGH

[3]Life Sciences Tata Consultancy Services Limited, Hiranandani Estate, Thane (W), Mumbai

[4]Dr. SHATAKSHI SRIVASTAVA

[4]Apeejay Stya University, Sohna, Gurugram

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INTRODUCTION

Urinary tract infection (UTI) is the second most common bacterial infections in adults as well as children (Foxman., 2003). It also accounts for healthcare associated infections and one of the most common nosocomial infections. In India, it is the third most prevalent infection (Saha et al., 2014) and frequents occurs in infants and children. Females are more prone to UTI compared to males (Kaur et al., 2014; Arvind et al., 2001).

The epidemiology of the infection variates with age, gender and other factors including genetic susceptibilities. The bacterial infection of UTI is categorised into two types based on site of localization of pathogenic bacteria in the urinary tract. It is categorised as uncomplicated (in case the pathogenic bacteria residing at urinary bladder) and complicated (the dispersion of the infection to ureters to kidneys and leading to kidney failure) (Noormandi et al., 2015).

The causative agents of urine infection involves both gram positive and gram-negative bacteria. Though, the gram-negative species are predominant. Commonly isolated gram-negative bacteria from the samples of infected individuals are Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, Klebsiella pneumonia, K.oxyntoca, Salmonella paratyphi, Citrobacter freundii, Vibrio cholera, Serratia marcescens, Providencia stuartii. Among these E.coli is the most common species (Bouamri et al., 2015; Bokil et al., 2011) responsible for causing community acquired and catheter associated urinary tract infections in both the genders (Linhares et al., 2013)(Floyd et al., 2015).

In order to resolve health and medical issues, there is a need to manage the transmission of uropathogens. The transmission of the infection occurs through routes of fecal, oral, contact, contaminated water, food and transplacental passage. The identification of these organisms is carried over by the conventional methods like non-culturing and culturing methods, enzyme linked immunosorbent assay, polymerase chain reaction, and isothermal microcalorimetry. The detection and diagnosis of these etiologic agents are of major interests and concerns globally. As the detection of these species are time consuming and fails accuracy often. Therefore, delayed detection led to lethal effects. Hence, in this practise introduction of biosensors is one of the promising approaches over the conventional methods.

BIOSENSOR BASED DETECTION OF UROPATHOGENS

In recent times the identification of causative agents of UTI using biosensor technologies proved to be rapid and sensitive. It is an attempt towards medical science

to utilize potential of biosensor-based detection methods more extensively (Yamada et al., 2016) (Sun et al., 2005) (Gaster et al., 2009). Advanced outcome of few biosensor-based methods practiced are summarised briefly in this manuscript.

Dual signal amplification via enzyme-based target recycling

In this approach, dual signal amplification unites with other methods to enhance the sensitivity for better outcome. It is nucleic acid based which coupled with enzymatic target recycling technique with the quantum dot (QD) layer-by-layer (LBL) gathered labels to obtain signal development and sensitivity instantaneously. The method is preferred as, recycling of DNA is based on target DNA sequence and utilize it several times follows with direct amplification and improves the signal. Combination of LBL and QD labels increase the sensitivity of the method (Deshmukh et al., 2013) (Hou et al., 2014; Fang et al., 2015; Cui et al., 2016).

Magnetoelastic sensor-based technology

This method is aptasensors based that involve magnetic beads to identify the targets. In this biosensing method, immunocomplexes are combined with aptamers. In of the research articles, it was reported that E.coli was detected using magnetic beads and measured the bacterial growth and susceptibility (Reverte et al., 2015) (Geng et al., 2011).

Electrochemical endotoxin sensors based on TLR-4/MD-2 complexes

Extensive use of electrochemical sensors is observed in the detection of microorganisms, bacterial DNA and RNA, lactoferrin in urine []. The approach of detection is based on immobilization of a human recombinant toll-like receptor 4 (rhTLR4) and myeloid differentiation-2(MD-2) complex which specifically bind to endotoxin (Shen et al., 2014), on gold electrodes through a self-assembled monolayer (SAM) technique. Interactions between the complex and endotoxins generate electrochemical signals and measured by cyclic voltammetry and differential pulse voltammetry (Yadav et al., 2016; Guerreiro et al., 2014).

APTAMER BASED BIOSENSORS

Aptamers are kind of synthetic oligonucleotides. They are capable of binding to hormone, proteins, or even whole cells at their specific target sites. Additional advantage of this method is that the process of detection can be done in vitro. Systemic Evolution of Ligands by Exponential Enrichment (SELEX) is effective detection method. In this, it gradually selects the aptamers by recurrent cycles of parting and preparing

copies from large random synthetic oligonucleic acid library (Nezlin., 2016). Apatamers are formed according to specific target DNA/RNA binding sites, and that has to be obtained from the whole library which is amplified and sequenced to get the aptamer. The advantages of this technology include easy formation, modified simply and highly stable (Guillén et al., 2012; Bunka et al., 2006).

Microcantilever array biosensors

There are three modes of operation of cantilever biosensors and are as follows (Simoni et al., 2015):

Dynamic or resonance mode- The chosen analyte molecules combines with molecules on functional layers of cantilevers, variating their chemical structures, adsorption, desorption or including binding or release of molecules from the function layers. The changes are observed as adsorbed mass followed by analysis of monitoring the resonance frequency of cantilever (Johnson et al., 2012).

Static mode- The perturbation in the analyte may arise variation in the composition of Cantilever's surface and lead surface stress on the part where reaction occurs and results cantilever to bend. The basic principle behind this method, is the measurement of the bending (Kim et al., 2015; Arlett et al., 2011).

Differential static mode- The static mode method, lack precise measurement of bending arise by analyte. Therefore, differential static mode of operation was another choice. In this mode, and an additional reference cantilever was utilized which does not counter with the analyte. Henceforth, compared to the static mode, this method gives accurate measurement of bending caused by the analyte (Boisen et al., 2009; Fritz., 2008).

Limulus amoebocyte lysate assay (LAL)

This biosensing method rapid, precise and highly sensitive in identifying endotoxin and used for vaccines, antibiotic products and blood products. LAL is application of the natural antibacterial defense mechanism or immune response of horseshoe crab (Limulus polyphemus) for the detection of endotoxins secreted by uropathogens. It is detected by the uropathogen infection leads to the clotting of its hemolymph (Noda et al., 2010; Chalupniak et al., 2014). The samples used for identification of the causative agents are blood sample, urine sample and any other body fluids.

CONCLUSION AND FUTURE PROSPECTS

Since 1960s the use of biosensor was introduced. Biosensor is extensively used in various fields like environmental monitoring, food and beverage industries, pharmaceutical industries, agriculture and medical fields (Lévêque et al., 2015). Past few decades, in the area of medical science as diagnostic approach it showed promising results. In diagnosis, biosensors act as bioreceptors such as antigens, antibodies, enzymes, nucleic acids, cellular structures and whole cells, or transducers such as optical, electrochemical and mass sensitive. These bioreceptors specifically bind the analyte of interest to be identified. In upcoming time usage of biosensor method of detection may lead to recognition of DNA, RNA and proteins of causative agents of the infection. The commercial implementation of this technology may be diversely used in aspect of other infectious diseases. The diagnostic approach will be preferred as it is labor intensive, time consuming, cost effective, portable, sensitive (minutue concentrations of biological samples can be detected) (Mach et al., 2011) (Mozaz et al., 2004). The method also reveals key parameters that determine the quality of the sample. Though, further studies are essential for expansion for identification of diverse microbial species involved disease causing and may followed to improving clinical management.