Biosensors Used in Dentistry: A Review

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Abstract

A bio-sensor is composed of six elements which include bio-receptor, transfusion element, chemically active interface, signal amplifier, signal processor and display. The analyze binds to the immobilized biological material and forms a product. The product linked change is then converted by the transducer into electric signals which can be amplified and measured. Oral fluid bio-sensors have the advantages of easy accessibility and noninvasive sample collection, making them a novel method in disease diagnostics. However, its limitations such as less sensitivity and specificity are overcome by the advent of new technologies such as microfluidics and nanofluidics. This review article discusses the concepts and applications of biosensors in the field of dentistry.

Keywords*: Biosensors, Types, Applications in Dentistry*

Introduction

Humans have been performing bio-analysis seeing as the sunrise of the time, utilizing the sensory nerve cells of the nose to detect scents or to detect the enzymatic reactions of the tongue to taste the food. Since biological organisms are the most efficient machines that are ever created, many scientists have an eagerness to apply as well as copy their efficiency to utilize it in man-made creations.[1] Scientists have developed a new means of chemical analysis by using bio-receptors from biological organisms that often have the highest selectivity of the biological recognition system. These bio-recognition elements when combined with various transfusion methods, created a rapidly expanding fields of bio-analysis as well as associated technologies that are known as biosensors.

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A bio-sensor is composed of six elements which include bio-receptor, transfusion element, chemically active interface, signal amplifier, signal processor and display.[2] The analyzer binds to the immobilized biological material and forms a product. The product linked modifications are then converted by the transducer into electric signals which can be amplified and measured.[3] This review article discusses the concepts and applications of biosensors in the field of dentistry.

Basic concepts of biosensors

A biosensor contains a sensor-element along with a bio-element. The bio-element may be an enzyme living cells, antibody or tissue. The sensing constituent may be an electric current, electric potential etc. This bio-element, as well as sensor-element, can be attached in one of the four possible customs like a membrane entrapment custom which is a semi-permeable membrane that segregates the bio-element where it is attached to the sensor.[4] The second one is a physical adsorption custom that is reliant on a combination of the van der walls forces, hydrophobic forces and hydrogen bonds as well as iconic forces to connect the bio-material to the exterior of the sensor. The third one is the porous

entrapment custom which is based on an encapsulation matrix formation around the biological material that helps in binding it to the sensor. And the fourth one is the covalent bonding custom has a sensor surface that is treated as a reactive group to which the biological materials can be attached.

Types of Bio-Sensors:

(A) Blood glucose bio-sensor - It is the biggest bio-sensor success story in commercial use for diabetes control. Rapid analysis forms a single drop of blood which is the analyzer that monitors glucose level in the blood.[5]

(B) A holographic bio-sensor - It uses holograms as sensing elements and it is used to screen pancreatic disorder by detecting trypsin in the duodenal fluid.[5]

(C) *Nanoshell bio-sensor* - It uses gold as a transducer, because of its high scattering level, so that sub nanograms/mm quantities of Ig in saline, serum and blood can be measured. It enhances chemical sensing by 10 billion times and is being urbanized for applications together with various cancer therapies as well as testing of proteins that associated with Alzheimer's disease.[5]

(D) *Bio-detector* - It is used for DNA sequences and mutation detection. Bio-detectors are faster than conventional PCR and also more efficient in producing the number of DNA copies.[5]

(E) *Immuno bio-sensor* - Used to detect Ag-Ab reaction for analysis of complex fluids to analyze micro-organisms, viruses, pesticides and industrial pollutants. They are designed for easy use by the untrained personnel.[5]

Components of a Bio-Sensor

There are 2 basic components of a bio-sensor:

(1) Biological component (a) Analyst (blood, serum saliva, urine and stools etc. (b) Sensitive bio-element created by biological engineering (enzyme, antibody, nucleic acids, cells and tissues etc).[6]

(2) *Physical component* (a) Detector transforms the signals that are being ensued from the interaction of the analyst with the biological element into other signals which are easily measured and quantified. (b)Amplifier/ display unit is the signal processors or the electronic component accountable for the display of the results in a user-friendly way.[6]

Role of oral fluid-based bio-sensors in dentistry:

Dental caries: Since dental caries is an irreversible multifactorial disease affecting the tooth, which often leads to cavitation, caries activity tests are performed to measure the caries activity which helps in motivating patients in caries prevention. However, caries activity tests consume a lot of time, and so to save the time of clinicians, a fiberoptic bio-sensor was developed to monitor tooth loss concerning *S. mutans* in human saliva. The finding of this bio-sensor confirmed that there is a decrease in absorbance of saliva with increased bacterial activity.[7] Hence this test can be used to monitor *S. mutans* activity in saliva as its levels correlate with dental caries.

Periodontitis: This is a type of chronic inflammation of the periodontal tissues caused by a continual bacterial infection that result in parameters such as probing pocket depth, bleeding on probing and loss of clinical attachment and radiographic assessment of bone loss provide information on the severity of periodontitis but not on disease activity. This need resulted in the development of biomarkers which can measure periodontal disease at the molecular, cellular, tissue and clinical levels. Several biomarkers associated with inflammation, soft tissue and bone destruction have been identified in GCF and saliva. IL-1B, MMP-8, TN F-A, IL-6 and C-reactive protein (CRP) are the biomarkers associated with periodontitis, for which saliva-based bio-sensors have been developed by a group. Another bio-sensors called the Integrated Micro-fluid Platform for oral diagnostics was developed which can detect biomarkers such as MMP-8 TN F-A, CRP and IL-6.[8]

Oral cancer: Oral cancer is the eighth most widespread cancer in men while it is fourteenth most common cancer in women worldwide. It is the most common cause of mortality and morbidity among the developing countries. Hence, for early detection and assessment of risk, various biological markers have been developed. The use of saliva-based bio-sensors for exfoliated cells in the oral cavity allows screening and identification of potential biomarkers for oral cancer. Besides, it can reduce anxiety and discomfort in the

patient compared routine biopsy techniques. Mi-RNA, are short non-coding RNAs encoded throughout the genome where some of these genomic regions are prone to alterations. An electrochemical bio-sensor method for the detection of oral cancer-related mi-RNAs at levels was developed which detects mi-RNA using a magnetic controllable gold electrode.[9] The advantage of this bio-sensor is magnetic beads-based enzymatic catalysis amplification which improves the sensitivity of bio-sensor.

Principles of detection

Bio-sensors work mainly via the following principles:[10]

(1) Photo-metric - Many of these optical bio-sensors are theorized on the phenomenon of surface plasma on resonance (SPR) which is an evanescent wave technique. This utilizes gold as an electrode. A photometric detection system is used to detect the optical signal.

(2) Electrochemical - Bio-sensors based on enzymatic catalysis of a reaction that produces or consumes electrons (the enzymes used for the catalysis are called redox enzymes).

(3) Piezoelectric - These acoustic devices utilize crystals undergo an elastic deformation when an electric potential is applied to them. The alternating current produces a wave in the crystal whose frequency is dependent on the elastic properties of the crystal.

(4) Thermal detection bio-sensor - Commonly used in the detection of pesticides and pathogenic bacteria, its high sensitivity to thermal changes without frequent calibration and intensity to optical and electro-chemical properties in the sample are some of its advantages.

Role of oral-fluid based bio-sensors in systemic diseases:

(1) DIABETES - Diabetes mellitus is a systemic disorder characterized by hyperglycemia, in which the patient should be regularly monitored to prevent further complications such as neuropathy, vascular diseases and predisposition to infection. For continuous monitoring of glucose levels, researchers have investigated the possibility of using GCF and saliva. The glucose level in saliva can be measured by a salivary nano bio-sensor which is an on-chip electrochemical sensing device. The charge transfer complex formed on the working electrode allows the direct oxidation of the glucose oxidase enzymes and thus determines salivary glucose levels.[11]

(2) *HUMAN IMMUNODEFICIENCY VIRUS* - It can also be used widely as a diagnostic tool for HIV and hepatitis C virus infection as it undergoes blood testing for Ab screening, particularly home testing. Electrochemical peptide sensors are fabricated for anti-HIV Ab detection which uses X-ray photoelectron spectroscopy to analyze salivary DNA on the sensor surface.[12]

(3) *PSYCHIATRIC DISORDERS* - Increased stress levels are observed due to change in lifestyle. This can lead to physical disorders such as cardiovascular, diabetes, obesity, and psychiatric disorders such as depression, schizophrenia, attention deficit and bipolar disorders. In saliva, cortisol and sAA are recognized as biomarkers for stress. A flow filtered ported, surface plasma on resonance (SPR) biosensor was developed to detect cortisol levels in saliva. In SPR bio-sensors, receptor molecules are immobilized on the gold sensor for detecting cortisol. For determining sAA levels, sAA bio-sensor is used which can act as a biomarker for autonomic dysregulation.[13]

(4) *DRUG ABUSE* - A serious problem with long term consequences. Illicit drugs can be detected in oral fluids, and in contrast to urine, they contain parent drugs rather than metabolites. Hence, they can be used as screening and confirmatory tests for illicit drug abuse. Lee et al developed giant magneto-resistive bio-sensors integrated with a portable reading system using competitive assays to trace tetrahydrocannabinol levels in saliva.[13]

Bio-sensors with saliva as an analyst:

(1) Bio-sensors using saliva help detect HIV-1, HIV-2, viral hepatitis, oral cancer, breast cancer, type-2 diabetes, periodontal disease and caries.[5]

(2) The oral fluid nanosensor test (OFNASET) is an automated, easy to use an integrated system that enables simultaneous as well as rapid detection of nucleic acid target and multiple salivary proteins. OFNASET

detector can also be used in the office of a dentist or another health care provider for various point-of-care disease screening and detection [14].

Applications of bio-sensors - cancer detection

a) Helps to spot cancer cells circulating in the blood either from a cancer patient, or treated tumour that has returned to the cancerous phase.[15,16]

b) Detects altered expression levels of micro RNAs, the new targets for cancer therapy, that are correlated with cancer type, tumour stage and response treatments.

c) Helps in detecting health-related problems associated with soft tissues including tendon and ligament, hard tissue as well as bone-related diseases such as osteoporosis and Paget's disease. [15,16]

Other uses:

A) Biosensors are used not only as diagnostic and prognostic tools in medicine but have various other uses[13]

B) Glucose monitoring in diabetic patients which is a historical market driver[2]

C) Pregnancy tests which detect the h CG protein in urine[1]

D) Estimates fracture risk and determine the response of bone to the treatment of bone disease[15]

E) Remote sensing of airborne bacteria example in counter-bio terrorist activities.

F) Determining levels of toxic substances before and after bio-remediation.[2]

G) Detection and determining of organophosphate.[17]

Conclusions

As bio-sensor technology advances a various range of applications broadens. Bio-sensors are now being made for the detection of microbial pathogens and their toxins, blood analysis, monitoring of glucose and other metabolites and other physiological monitoring and cancer detection. Oral fluid bio-sensors have the advantages of easy accessibility and noninvasive sample collection, making them a novel method in disease diagnostics. However, its limitations such as less sensitivity and specificity are overcome by the advent of new technologies such as microfluidics and nanofluidics. It is almost certain that in the forthcoming years home testing kits incorporating oral fluid bio-sensors will begin to appear, outperforming the routine laboratory tests in the diagnosis of disease.

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