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Review Article

Biosensors used in dentistry – A Review Article

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ABSTRACT:

BIONSENSORS are 'simple to use' gadgets devised in the early detection and treatment of illness. Many illnesses can be effectively treated if they are detected early. Biosensors detect a targeted molecule which later transmits an electrical indication by utilising the unique features of biological and physical materials. It has two major advantages: quick reaction and great sensitivity. The combination of nanomaterials, microfluidics, automated samplers, and transduction devices on a single chip would also be a major benefit for point-of-care devices like Biosensors. They are also being employed in medical research as an on-site-screening (OSS) device which would play a serious role in the easy, quick, and early detection of various diseases including oral cancer. This review summarises the benefits of biosensors in various applications in dentistry.

Keywords: Oral Biosensor, Dentistry, lab-on-chip devices.

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INTRODUCTION

The recognition of bio-analysis dates long back, starting from detecting odours with sensory nerve cells in the nose and tasting food with enzymatic reactions in the tongue. Our understanding of the role of living creatures in sensing tiny levels of bio-chemicals in complex systems has grown as time passed.[1]Researchers have devised a novel technology of analysis using chemicals that uses bio-receptors from living organisms or receptors formed after biological reactions, they have greater selectivity to biological recognition systems.[2] These biorecognition elements, in combination with various transduction mechanisms, have aided in the development of bio-analysis and associated technologies such as biosensors and biochips.[3]

Nanotechnology is paving the way for the creation of nano-sensors and nanoprobes with submicron-sized dimensions that may be used for measurements of intracellular elements. Although it is hard to cover every aspect of this fast-moving subject, this review highlights a variety of biosensors and its applications in various field of dentistry.[3]

METHOD OF COLLECTION OF DATA

Extensive literature search in various search engines were done and key words such as oral biosensors, biosensors, point of care systems were used and related articles were collected for structuring the review.

WHAT IS A BIOSENSOR?

According to the International Union of Pure and Applied Chemistry (UPAC) “a biosensor is a device that uses specific isolated enzymes-mediated biochemical reactions to detect chemical compounds either by thermal, electrical or optical signals”[4]

BIOSENSORS DEVELOPMENT - HISTORY

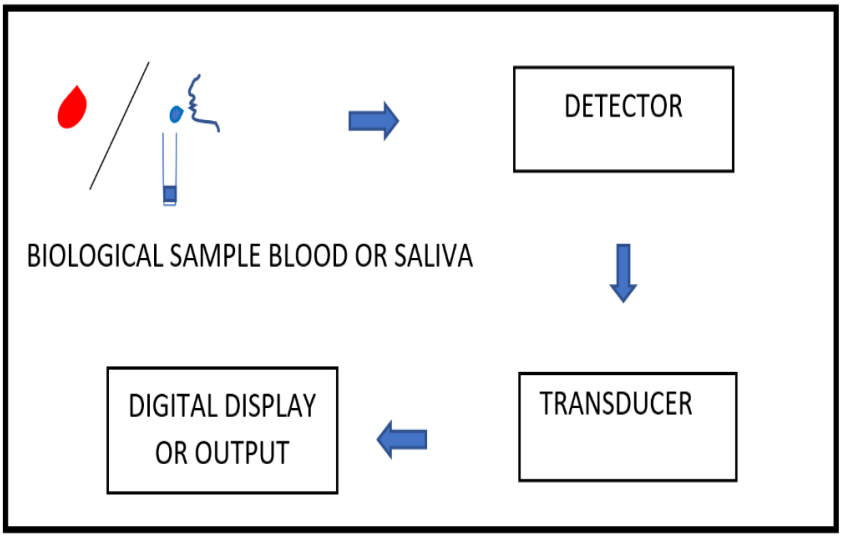
Dr. Leland C Clark invented the first biosensor in 1960s, utilising an "enzyme electrode" to measure glucose levels using Glucose Oxidase (GOD) enzyme. Later integrated multi-analyte sensors were invented by doing extensive studies, in which a single device was developed for glucose, lactate, and potassium

detection. Further a miniaturized integrated biosensors was developed for determining glucose, lactate, and urea in micro samples of undiluted whole blood or plasma.[5,6,7]

THE FOLLOWING ARE THE MAIN COMPONENTS OF A BIOSENSOR:

1. A biomolecule identifier which would invoke a stimulus
2. A transducer to convert the stimulus into an output signal
3. A signal processing system to interpret the output signal and present it in the readable form.[8]Fig.1

Figure 1: Figure showing components of a biosensor



PRINCIPLE OF BIOSENSORS

The biosensor works in many ways but one of the usual methods of working is the immobilisation of biological material when dispersed on to the device and binds to the analyte and creates a product. The transducer then transforms the product-linked changes into electric fmonitor and control system after processing.[9]

TYPES OF BIOSENSORS

According to the type of biorecognition component and transduction element used the biosensors can be categorized (antibodies [Ab], enzymes, nucleic acids, and entire cells) or their transduction elementused for detection. (Electrochemical, electric, optical, piezoelectric, and thermal). The various biological component and transduction elementused is listed in Table1.[10]

Table1: Tabular column showing the various biorecognition component and transduction element of biosensors.

Biosensor	
Biorecognition component	**Transduction element**
- Antibodies - Enzymes - Nuclei acids - Entire cells	- Electrochemical - Electric - Optical - Piezoelectric - Thermal

The various transduction methods used in biosensors are amperometric, potentiometric, conductometric, ion-sensitive, fluorescence, surface plasmon resonance (SPR), chemiluminescence, bioelectrical wire (BW), surface acoustic wave (SAW).The different types of biosensors along with transduction element and their principle is summarized in Table2.[11]

Table2: Tabular column showing the various types of biosensors along with the transduction element and their principles.

Biosensor	Method of transduction	Detection principle
1. Electrochemical	Amperometric	It measures the current that is created when electroactive substances are reduced or oxidised during a biological reaction.
	Potentiometric	It determines the potential difference between a working electrode and a second reference electrode when there is no current flowing.
2. Electrical	Conductometric	It evaluates how the presence of the analyte affects the system's conductance.
	Ion-sensitive	It determines the changes in surface electrical potential caused by ion interactions with the semiconductor.
3. Optical	Fluorescence	It is based on the fluorescence emission processes involved in the photophysical principles.
	SPR	It measures the rise in refractive index that takes place when one of the interacting partners attaches to its ligand that is immobilised on the surface of an SPR sensor substrate.
	Chemiluminescence	It is based on the energy of a chemical reaction which may be evaluated as the light gets emitted.
4. Piezoelectric	BW	It measures the mass shift that affects the transacoustic wave's vibrational frequency as it moves from one crystal face to another.
	SAW	It measures a mass shift that modifies the vibrational frequency of an acoustic wave moving from a single crystal face.
5. Thermal		A biological reaction's heat is measured at the sensing component.

VARIOUS BIOSENSORS USED IN DENTISTRY

DENTAL CARIES DETECTING SENSORS

The oral wearable sensors also referred as dental sensors, are sensors which are intended to track crucial dental parameters where dental diseases can be diagnosed and treated at an early stage. The most common chronic dental disease is dental caries.[12] The conventional approaches for detecting dental caries rely on the independent construal of visual inspection and tactile feeling, along with a radiograph as a support. Dentists should be aware that dental caries might be challenging to detect and diagnose in the early stages since it is a chronic condition. Dental caries is sometimes not observed in regular practise until a cavity or degraded surface manifests, which is an indication of a fairly severe condition. This suggests that a real-time oral wearable sensor for monitoring dental health is very necessary.[12,13]According to literature the production of volatile sulphur compounds locally is a result of anaerobic bacteria degrading sulphur-containing proteins which may be highly linked to concealed dental caries. Monitoring the release of volatile sulphur components may allow for the preliminary diagnosis of the concealed dental caries. In order to track and find dental cavities, a study conducted by Y. Li et al.[16] recently unveiled a wearable fluorescent mouth guard based on zinc oxide quantum dots/poly (dimethyl siloxane) (ZnO/PDMS) nanocomposite. The fluorescent probe used in the study were, ZnO quantum dots, which typically exhibits intense yellow fluorescence under UV light and which would undergo considerable fluorescence quenching when in contact with volatile sulphur compounds.[14,15,16]

PERIODONTITIS

Periodontal disease is a significant risk factor for heart and cerebrovascular disease. Periodontitis is indicated by a number of clinical parameters, including pocket depth, bleeding, clinical attachment level and radiographic evaluation of bone deterioration.[17,18,19] Biomarkers play a critical role in evaluating periodontal diseases at the cellular and molecular levels. Saliva and Gingival cre vicular fluid (GCF) have been discovered to include a number of indicators linked to inflammation of soft tissue and bone deterioration. The biomarkers are Interleukin-1β, Matrix metalloproteinase (MMP-8), Tumour necrosis factor-α (TNF- α), Interleukin-6 and C-Reactive protein (CRP).However, no one indication is enough to provide a conclusive diagnosis.[20]

DENTAL FLUOROSIS

The most accurate and sensitive devices for identifying and assessing dental fluorosis are optical

biosensors. It has several uses in the field of biomedical, healthcare and medical research. For instance, the nature of drinking water is directly impacted by the quantity of fluoride in groundwater. A 2-dimensional photonic crystal-based biosensor with line flaws has been shown to be capable of detecting different fluorides and their levels in water. The resistor in the biosensor is very sensitive and can also detect minute variations by a minor shift in frequency caused by band formation. In the probe technology the calcium fluoride, caesium fluoride, potassium fluoride, lithium fluoride, and strontium fluoride compounds were used and were shown to produce a peak in the fluoride concentration. It can serve as a very useful tool for identification of dental fluoros is brought on by the fluoride in water. In various studies the testing was conducted using the Finite-difference Time-domain (FDTD) approach.[21]

MONITORING OF ORTHODONTIC MANAGEMENT

The goal of orthodontic therapy is to move and rotate the tooth in the bone. During treatment, alterations can be made on the pressures subjected to the teeth by orthodontic appliances. Dental pulp, bone and periodontal tissue are all at danger if inappropriate pressures and moments are applied to the teeth. Lapatki et al.[22] had developed a "smart bracket" to determine the various force-moment components of wires and brackets on a single tooth. In one chip multiple sensors were incorporated via a complementary semiconductor made of metal oxide (CMOS). In the bracket base the chip was placed. The force-moment was measured and could be reconstructed. There are some drawbacks of this sensor as when applied to multiple teeth large data would be detected which needs to be managed.[22,23]

DENTAL IMPLANTS- MONITORING

Dental implants are replacement of missing tooth, these would be surgically inserted into the bone to simulate the function of tooth. Therefore, we have come under scrutiny to increase the feat of dental implants and lengthen their useful life due to their high cost and unpleasant treatment method. In general, the creation of strong anchorage to bone is a direct organizational link amid bone surround the implant surface at the optical microscopic level which determines whether dental implants will be successful or not. However, X-ray imaging, is currently the only major method used to gather inside information regarding the growth of bone surrounding the implant. The same can be assessed using a capacitive sensor, the sensor is made of Cu-Poly-ether-ether-ket one (PEEK), and the density and development of the bone around the implant was assessed. The sensors capacitance would eventually decrease from its original value while the osseo integration process and bone development occurs. The data recorded from the capacitance will be then wirelessly sent to the exterior device and changed to a format that dentists could interpret. The advantage of this sensor is that its capacitance was selected as an easily observable indication to continuously express the state of bone anchoring with little power consumption and wireless transmission. However, it should be noted that the sensor cannot be removed following effective bone anchoring, and its possible negative long-term implications should be carefully examined.[24,25,26]

ORAL CANCER DETECTION

Oral cancer is the eighth most common cancer occurring worldwide. The occurrence of cancer is maximal among the males. It is one of the most frequent causes of mortality and sickness in people in developing nations.[26] The various salivary biomarkers used for early detection and risk assessment are Interleuikin-8 (IL-8), Tumour necrosis factor- α (TNF-α), Epidermal growth factor receptor (EGFR) and microRNA (miRNA) such as transferorin and genome.[27]Table 3 shows the tabular column summarizing the various biosensors used in the field of dentistry.

Table3: Tabular column showing biorecognition materials used in various applications of dentistry

1. Dental caries	Volatile sulphur compounds (Oral wearable dentures)
	To test the saliva to monitor Streptococci activity. Salivary α-Amylase (sAA) enzyme in colorimetric biosensor for detection of dental caries.
2. Periodontitis	Can be detected in both saliva and GCF (gingival crevicular fluid) . - Interleukin-1β - Matrix metalloproteinase (MMP-8) - Tumour necrosis factor-α (TNF- α) - Interleukin-1β - C-Reactive protein (CRP).
3. Dental 4. fluorosis	The following compounds to be detected in water content to cause dental fluorosis: - CaF (Calcium fluoride) - CsF (Caesium fluoride) - KF (Potassium fluoride)

		- LiF (Lithium fluoride) - SrF_2 (Strontium fluoride)
5. Orthodontic treatment management		"Smart Brackets" can be used to detect the force-moment on the teeth applied.
6. Dental implant monitoring		Capacitive biosensor - Cu-Poly-ether-ether-ketone (PEEK)
7. Oral cancer	Early detection	Biomarkers used are: - Interleukin-8 (IL-8) Tumour necrosis factor- α (TNF-α)
	Tumour angiogenesis and metastasis	- Epidermal growth factor receptor (EGFR) - microRNA (miRNA) - Cell free DNA (cfDNA) - Interleukin-8

THE VARIOUS OTHER APPLICATIONS WHERE BIOSENSORS USED ARE

1. Hyperglycaemia: Diabetes mellitus is a disorder rather than a disease. Which is usually characterized by high levels of glucose in blood. The prolonged exposure of diabetes can lead to various systemic complications such as neuropathy, nephropathy and vascular disorders. Therefore, there is a continuous need for monitoring of blood glucose levels. The blood glucose levels can be assessed using GCF and saliva. A salivary nano biosensor with electrochemical sensing device can be used for regular evaluation of glucose levels.[28]
2. Viral infection: Infections like HIV (Human Immunodeficiency Virus) and Hepatitis-C (Hep-C) can be detected using a biosensor. In an electrochemical peptide sensor, a specific antibody can be used along with X-ray photoelectron spectroscopy to analyse salivary DNA in the surface of the sensor.[29]
3. Psychological disorders: In psychological disorders the stress levels fluctuate drastically, which is majorly influenced by the sedentary lifestyle and can lead to various systemic diseases such as cardiovascular disorders and also various other psychological disorders such as depression, schizophrenia and bipolar disorders etc. During severe stress certain biomarkers are released in saliva such as cortisol and Salivary α-Amylase (sAA). Surface plasma on resonance (SPR) biosensor with flow filtered ports can be used to measure salivary cortisol levels. Receptor molecules are adsorbed on the gold sensor in SPR biosensors for cortisol and sAA detection.[30]
4. Drug abuse detector: A significant issue with long-term effects of drug abuse can be identified using oral fluids. Unlike urine, the oral fluids do not include much metabolites but may contain predominantly the parent drugs. As a result, they can serve as both screening and confirmatory tests for drug misuse. To track tetrahydrocannabinol levels in saliva, enormous magneto-resistive biosensors combined with a portable reading apparatus can be used to detect drug misuse.[30]

CONCLUSION

The spectrum of uses for biosensor technology is expanding. Today, bio-sensors are being developed for a variety of physiological monitoring applications, including the uncovering of microbial infections and their toxins, blood analysis, glucose and other metabolite monitoring, and cancer detection. Oral bio-sensors are a unique tool for diagnosing diseases because of their advantages of being easy detectable and non-invasive sample collecting. New technologies like microfluidics and nano fluidics have, however, solved its drawbacks, such as a lack of sensitivity and specificity. Home testing kits with oral fluid bio-sensors will likely start to develop in the upcoming years, surpassing standard laboratory tests in the detection of illness.

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AUTHOR CONTRIBUTIONS

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

COMPETING INTERESTS

Authors state no conflict of interest.

ETHICAL APPROVAL

The local Institutional Review Board deemed the study exempt from review.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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