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A REVIEW ON THE APPLICATION OF HYDROGEL BASED SENSORS FOR BIOMEDICAL

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Abstract

In recent years, biosensors that identify and transform biochemical processes to a detectable signals have gained a lot of interest. More than 150,000 papers covering the application of biosensors in multiple industries were reported around 1950 and 2017, but important reports describing hydrogel-based biosensors for biomedical applications are uncommon to the best of our understanding and without diligent screening. The biomedical application of hydrogel-based biosensors is addressed in this study, based on a search conducted over the years 2000-2017 through the Network of Science Core, PubMed (NLM) and Science Direct online databases. We considered bioreceptors to be immobilised on hydrogel-based biosensors, their benefits and drawbacks, and strategies of immobilisation in this study. Along with the prevailing transduction strategies, we characterise the hydrogels that are most preferred for this form of biosensor. Biomedical applications of hydrogel-based biosensors are explained, involving cell metabolite and pathogen identification, tissue engineering, wound healing, and cancer tracking, and techniques are established for the identification of tiny biomolecules such as glucose, lactate, urea, and cholesterol.

Keywords: *Bioreceptors, Biosensing, Biomedical, Cancer, Hydrogen Gels.*

I. INTRODUCTION

In recent years, biosensors that identify and transform biological reactions to a detectable signal have gained a lot of interest. Biosensors provide a measurable signal produced by chemical reactions by the combination of a biologically active portion with a suitable transducer. As a molecular species, a bioreceptor uses a biochemical pathway for communicating with the analyte, like nucleic acid, enzyme, antibody, gene, or a biological system, including a cell or kidney. A transducer generates a detectable signal equal to the interaction of the bioreceptor-analyte. Bioreceptors are combined with base materials using multiple immobilisation strategies. Metals, polymers, glass, or composites may be made up of base materials[1].

In addition, because of their excellent physicochemical, mechanical, electrical, and optical properties, hydrogels as a swell-capable polymer with enviro-sensitive properties have a significant effect on a wide variety of applications. Hydrogels have regarded as a prominent medium with unexpected and tremendous potential for medicinal application, considering the time since their first discovery in 1968. Their implementations are still in the development process in this area[2].

The goal of this analysis is to summarise the biomedical applications of hydrogel-based biosensors, particularly bioreceptors explicitly suggested for hydrogels, immobilisation methods, sensor architecture and structural improvements, to recognise the possible functions of hydrogels for biological applications, and to propose implications for improvement studies[3].

II. DISCUSSION

A. **Bioreceptors: -**

Bioreceptors are elements of biomolecular detection that are responsible for linking a particular substance of importance inside a biosystem framework. While various different articles that have been activated for sensing can be tracked by several types of bioreceptors, they can be grouped into five different major categories. Y-shaped, complex proteins used to recognise foreign antigens, viruses, and bacteria are antibodies. Antibodies in biosensors have been used for various binding capabilities. Table 1 is representing the various advantages and disadvantages of bioreceptors.

Bioreceptor	Advantages	Disadvantages
Antibody	The immunogen need not be purified prior to detection.	Expensive and time-consuming method. Miniaturized immune-PCR detection methods have not yet been commercialized[4].
Enzymes	Variety of reaction products arising from the catalytic process.	Stability problems have been reported. The detection limits can be very low due to signal amplification[5].
Nucleic Acids	Target molecule can be recognized by shape and	It is not easy to design donor/acceptor labeling strategies.

	sequence. A wide range of biomolecules can be detected. High binding affinity, simple synthesis method and easy storage have been reported	They are sensitive to pyrimidine specific nucleases that are abundant in biofluids[6].
Cells	Can be used over prolonged periods of time as cells are closed systems.	[7]
Biomimetic	Known as an effective, accessible and inexpensive strategy. Physically, very stable (solid-like). The molecular imprinted polymers can survive in destructive environments.	Molecular imprint probes do not have the same flexibility and selectivity as actual bioreceptors[8].

Table 1 Advantages and Disadvantages of Bioreceptors

B. **Hydrogels for Biosensing: -**

As a special property of a particular geometrical structure, the "lock and key fit" is the capacity that an antigen-specific antibody demonstrates when used as a biosensor. Animal immune system exploitation is a typical method of producing polyclonal, monoclonal, and recombinant antibodies, of which polyclonal antibodies are famous for their regular use as immune sensors. Recombinant antibodies, including haptens, proteins, and carbohydrate moieties, have been designed to reflect structurally complex antigens.

Hydrogels are generated by chemical (covalent bonds) or physical (non-covalent interactions) crosslinking as water-swellable three-dimensional structures. These wise, highly biocompatible materials are known to increasingly communicate with biosystems, but suffers from adverse effects. For biomedical application, several features have made them popular: contact with biological systems at the molecular level; their regulation of viscoelastic properties; being reactive to external stimuli; possessing antifouling properties; and the presence of a broad variety of well-known methods for the synthesis to integrate bioreceptors into their extremely wet framework. In two ways, hydrogel-based biosensors can track biological events. The first involves bioreceptor-free hydrogels whom swelling properties alter in reaction to chosen biological activities. In this category, ionic hydrogels including environmental awareness, such as pH, temperature, and electric field, have been commonly used. In reaction to sufficient ionic strength modifications in the surrounding aqueous biosystem, pH-sensitive hydrogels either accept or emit protons. The further ionised ionic hydrogels are, the more electrostatic repulsion can be produced between polymeric chains, resulting in a negative or positive swelling ratio. In reaction to an electric field, the very same scenarios was reported for polyelectrolyte gels, the strength of which was accountable for the swelling and de-swelling mechanism. The larger the strength of the electrical field, the more variable charges which influence the swelling capacity may occur. A thermo-responsive hydrogel may be introduced by a copolymer of hydrophobic and hydrophilic monomers, where the ratio of the monomers in reaction to changes in biosystem temperature is accountable for phase transition. The biological interactions in a biosystem trigger swelling modification, besides the reasons listed for phase change, and may convert to a macroscopic response. The macroscopic response therefore has to use for biosensors as optical, conductometric, amperometric, or mechanical readings.

The second means of detecting biological events includes hydrogel-based biosensors that can handle bioreceptors for the identification of biochemical or biological associations, with regard to hydrogel porous structures and their special large internal surfaces. With this approach, bioreceptors immobilised by hydrogel are used to host component of biomolecular recognition to detect a specific biosystem case. Stable immobilisation of bioreceptors, surface attachment techniques, prevention of non - specific protein adsorption to the hydrogel surface, probe density, stability, and swelling kinetics are of great significance for developing this form of biosensor[9].

C. **Biomedical Applications of Biosensors: -**

Various trials, scientific studies, and advances related to the physical, chemical, mechanical, and biocompatibility characteristics of stimulus-sensitive hydrogels have led to our awareness of their new capacity in medical and biomedical applications for biological signal sensing. The use of biosensors to detect physiochemical changes in the body offers early diagnosis, care and control resources for illness (Fig. 1). Although some precision constraints, substantial progress has been made in developing advanced biomaterials that enable the design and development of a new generation of biosensor, reducing imprecision and sluggish reactions to physiological environments for improved therapeutic results. The efficient incorporation of tiny bioreceptors with sensing materials, a crucial step towards miniaturisation, has also facilitated the task of biosensing more advanced and appealing[10].

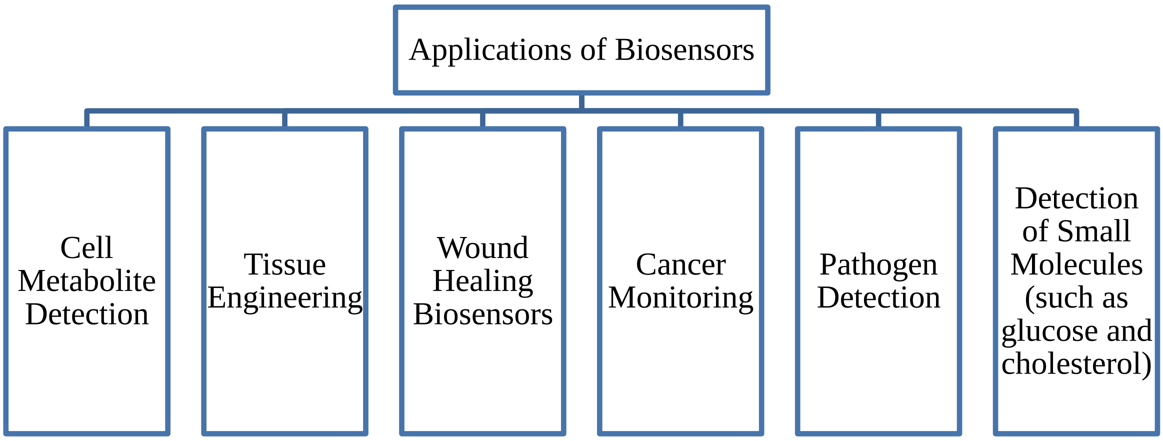

Fig. 1 Application of Biosensors

III. CONCLUSION

This thesis addressed the biomedical use of hydrogel-based biosensors. Different hydrogels were associated with biosensing skills. Polyvinyl alcohol, polyethylene glycol, polyacrylate groups, and electroconductive hydrogels are the most commonly utilized hydrogels. Biologically sourced hydrogels involve alginate, chitin, chitosan, agarose, dextran, cellulose, and hyaluronic acids. There was discussion of bioreceptors to be immobilised on hydrogel-based biosensors, their benefits and drawbacks, and strategies of immobilisation. Our research found that hydrogel-based biosensors are being used for various biomedical applications, as well as the identification of cell metabolites and bacteria, tissue engineering, wound healing, cancer screening, and small biomolecules like glucose, lactate, urea, and cholesterol identification techniques. In truth, 3D swelling of electrical signalling hydrogels, their permeability to different molecules and negligible contact with different swelling media, and also their capacity to optimally immobilise various biomolecules, indicate the function in the manufacturing of biosensors in the future. Some restrictions, involving lifespan, handling, and transducer adaptation for rapid quantitative analysis, show that hydrogel-based biosensors still have a long way to go before they are used in commercialised health management systems. In the meantime, targeted cell are labelled to grant the signal enhancement provided by biosensors which results in improvement evaluation. This method, though, is a possible source of difficulty, experimental error, and confusion that may put biomolecules at risk of property alteration. In biosensor processing, indirect costs are also included. To make this system most reliable, further cost-effective, easier, and much more responsive, replacing label-free biosensing approaches is indeed important. In the multi-target detection capabilities of the latest generation of biosensors, more substantial improvement is needed to provide a wide-ranging identification of objectives on a single measurement device.

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