RECENT ADVANCES IN BIOSENSOR TECHNOLOGY

Editors:
Vivek K. Chaturvedi
Dawesh P. Yadav
Mohan P. Singh

Bentham Books

Recent Advances in Biosensor Technology

(Volume 2)

Edited By

Vivek K. Chaturvedi

Department of Gastroenterology
Institute of Medical Sciences, Banaras
Hindu University, Varanasi, Uttar Pradesh
India

Dawesh P. Yadav

Department of Gastroenterology
Institute of Medical Sciences, Banaras Hindu University
Varanasi-221005
India

&

Mohan P. Singh

Centre of Biotechnology
Institute of Interdisciplinary Studies
University of Allahabad
Prayagraj-211002
India

Recent Advances in Biosensor Technology (Vol. 2)

Editors: Vivek K Chaturvedi, Dawesh P. Yadav and Mohan P. Singh

ISSN (Online): 2972-4082

ISSN (Print): 2972-4074

ISBN (Online): 978-981-5136-41-8

ISBN (Print): 978-981-5136-42-5

ISBN (Paperback): 978-981-5136-43-2

First published in 2023.

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Pte. Ltd.
80 Robinson Road #02-00
Singapore 068898
Singapore
Email: subscriptions@benthamscience.net

BENTHAM
SCIENCE

CONTENTS

FOREWORD

In 1962, when the term "biosensor" was first introduced by Leland C. Clark and Champ Lyons by describing the use of an enzyme-based electrode for measuring glucose levels, people did not think that it would revolutionize the next-generation medicines. Biosensors are one of the groundbreaking and promising innovations. Therefore, detailed information on them is paramount for budding students and researchers. With great pleasure, I introduce the notable book "Recent Advances in Biosensor Technology." In this rapidly evolving era of science and technology, biosensors significantly transform the landscape of science and technology, healthcare and the environment to safety, toxicity and beyond. The area is witnessing an unprecedented expansion of biosensor applications, driven by breakthroughs in materials science, nanotechnology, and bioengineering. This book is a comprehensive compilation of modern research and cutting-edge developments in biosensor technology. It synthesizes the expertise and contributions of leading scientists, engineers, and researchers, offering a unique opportunity for readers to delve into the frontiers of this exciting domain. The chapters within this volume encompass a wide range of biosensor-related topics, providing an insightful exploration of various biosensing principles, design methodologies, and real-world applications. As we explore the contents of "Recent Advances in Biosensor Technology," we will have the opportunity to learn the most recent and significant advancements in nanomaterials, bio-molecular recognition elements, signal transduction mechanisms, and data analysis techniques. Whether a reader is a researcher, a student, or an industry professional, this book is a vital resource, bridging the gap between theory and practice. The authors' dedication has resulted in a compilation that will lead the future of biosensor technology and its societal impact, reflecting the limitless possibilities. I extend my heartfelt gratitude to the contributing authors for their dedication and commitment to sharing their knowledge with the scientific community. Their collective efforts have resulted in a remarkable compendium that will undoubtedly shape the future of biosensor technology and its impact on society. In conclusion, "Recent Advances in Biosensor Technology" proves the brilliance of human ingenuity and the boundless possibilities that lie ahead. I wish you to discover the same level of inspiration and enlightenment in this book I experienced.

Gyaneshwer Chaubey
Department of Zoology
Institute of Science
Banaras Hindu University
Varanasi-221005
India

PREFACE

Currently, there are urgent worldwide demands for biosensor development for human health. The development of biosensors by researchers is enhancing day by day by increasing their sensitivity and affinity towards the biomarkers. The role of nanotechnology is economical, reliable and a novel approach to diagnosis and therapeutics. Nanotechnology-based sensors are used for fast, ultra-sensitive and economical diagnostics. Nowadays, the coating of carbon-based and non-carbon-based nanomaterials such as graphene, nanoparticle or quantum dot is being used on the electrode surface to increase the signal amplification of biomarker load. Organic coating of Quantum dots changes nanoparticles into the hydrophilic compound to connect DNA, RNA, proteins, peptides and other molecules. In carbon-based nanostructures, graphene oxide is biocompatible and has the ability for immobilization of nanoparticles and single-strand DNA. CNTs play a key role in biosensors preparation that can detect target molecules in very little amounts. Silica-based electrochemical biosensors have a wide surface area, stability in critical thermal and chemical conditions and good compatibility with proteins. Nowadays, silver, gold and metallic nanoparticles have been extensively used in the field of virus detection owing to their unique optical, electrical properties, catalysis activity, and magnetic resonance imaging.

In this book, we covered several chapters regarding biosensors in the identification and characterization of natural bioactive compounds present in the food, pharmaceutical, agricultural, environmental, and industrial sectors. This book also demonstrates the types of biosensors (enzymatic, wearable and paper based) that integrate with the human body in the form of tattoo, gloves, and clothing that help in monitoring human health by calculating their daily routine. It is simple to do painless evaluations of bodily fluids using various biochemical markers such as spit, sweat, skin, and tears. This includes the 3d bioprinting of advanced bioinks for bone tissue regeneration; in addition, microfluidic technology, organ-on-a-chip, and electrospinning technology are used to produce biosensing products for the diagnosis and monitoring of living systems. This book comprises several new efficient biosensors that play a crucial role in the diagnosis revolution in neurodegenerative diseases, covid-19 pandemic, microorganisms, gastrointestinal diseases, diabetes management, as well as in agriculture. Thus, this book aims to broaden the readers' (academicians, students, and researchers) horizons and guide them in tailoring different biosensing techniques for specific diagnostic procedures. This book highlighted the latest development and the significant role of different new biosensors in future technology.

Vivek K. Chaturvedi
Department of Gastroenterology
Institute of Medical Sciences, Banaras
Hindu University, Varanasi, Uttar Pradesh
India

Dawesh P. Yadav
Department of Gastroenterology
Institute of Medical Sciences, Banaras Hindu University
Varanasi-221005, India

Mohan P. Singh
Centre of Biotechnology
Institute of Interdisciplinary Studies
University of Allahabad
Prayagraj-211002
India

List of Contributors

Abhay Dev Tripathi	School of Biochemical Engineering, Indian Institute of Technology (Banaras Hindu University), Varanasi-221005, India
Abha Mishra	School of Biochemical Engineering, Indian Institute of Technology (Banaras Hindu University), Varanasi-221005, India
Alma Tamunonengiofori Banigo	Department of Developmental Bio Engineering, Faculty of Science and Technology and TechMed Centre, University of Twente, Drienerlolaan 5, 7522 NB Enschede, The Netherlands
Anand Maurya	Institute of Medical Sciences, Faculty of Ayurveda, Department of Medicinal Chemistry, Banaras Hindu University, Varanasi, 221005, Uttar Pradesh, India
Anurag Kumar Singh	Centre of Experimental Medicine & Surgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, Uttar Pradesh, India
Avanish Kumar Shrivastav	Department of Biotechnology, Delhi Technological University, Delhi, 110042, India
Bhaskar Sharma	Neurobiology Laboratory, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, 110029, India
Chinedu Chamberlin Obasi	Department of Pharmaceutical Biotechnology, Institute of Pharmacy, Martin Luther University, Halle-Wittenberg, Germany
Divya Mishra	Centre of Bioinformatics, University of Allahabad, Prayagraj, Uttar Pradesh 211002, India
Dhitri Borah	Department of Zoology, Biswanath College, Biswanath Chariali,784176, Assam, India
Dawesh P. Yadav	Department of Gastroenterology , Institute of Medical Sciences, Banaras Hindu University , Varanasi-221005, India
Gaurav Mishra	Institute of Medical Sciences, Faculty of Ayurveda, Department of Medicinal Chemistry, Banaras Hindu University, Varanasi, 221005, Uttar Pradesh, India
Himani Yadav	Department of Botany, University of Delhi, Delhi-110007, India
Hemant Arya	Department of Biotechnology, Central University of Rajasthan, Ajmer, Rajasthan 305817, India
Marjan Talebi	Department of Pharmacognosy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Manmath Kumar Nandi	Institute of Medical Sciences, Faculty of Ayurveda, Department of Medicinal Chemistry, Banaras Hindu University, Varanasi, 221005, Uttar Pradesh, India
Mohan P. Singh	Centre of Biotechnology, Institute of Interdisciplinary Studies, University of Allahabad, Prayagraj-211002, India
Mridula Chaturvedi	Amity Institute of Biotechnology, Amity University Noida, Uttar Pradesh, India

Neelesh Kumar	Department of Biotechnology, Delhi Technological University, Delhi, 110042, India
Prem L. Uniyal	Department of Botany, University of Delhi, Delhi-110007, India
Priti Giri	Department of Botany, University of Delhi, Delhi-110007, India
Praveen Rai	National Institute of Plant Genome Research, New Delhi, India
Ravi Kumar Goswami	Department of Zoology, Hindu College, University of Delhi, New Delhi-110007, India
Rajendra Awasthi	Department of Pharmaceutical Sciences, School of Health Sciences and Technology, University of Petroleum and Energy Studies (UPES), Energy Acres, Bidholi, Via-Prem Nagar, Dehradun – 248 007, Uttarakhand, India
Soumya Katiyar	School of Biochemical Engineering, Indian Institute of Technology (Banaras Hindu University), Varanasi-221005, India
Sushil Kumar Dubey	Centre of Biotechnology, University of Allahabad, Prayagraj, Uttar Pradesh 211002, India
Sujeet Singh	Department of Biotechnology, Central University of Rajasthan, Ajmer, Rajasthan 305817, India
Tejveer Singh	Translational Oncology Laboratory, Department of Zoology, Hansraj College, University of Delhi, New Delhi, Delhi-110067, India
Vivek Kumar Pandey	Department of Pharmacology and Nutritional Sciences, University of Kentucky, Lexington, Kentucky, USA
Vivek K. Chaturvedi	Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

LIST OF ABBREVIATIONS

ALG	Alginate
AM	Additive manufacturing
BBV	Bio-blood-vessel
BME	Biomedical engineering
BrCa	Breast cancer gene
CAD	Computer-aided design
CPF-127	Chitosan-g-pluronic F-127
CT	Computed tomography
3D	Three-dimension (al)
^{0}C	Degree Celsius
DCvC	Dynamic covalent chemistry
DN	Double network
DNA	Deoxyribonucleic acid
EB	Extrusion-based
EBB	Extrusion-based bioprinter
ECM	Extracellular matrix
GelMA	Gelatin methacrylamide
Gel-PEG-TA	Gelatin-Polyethylene glycol-tyramine
hMSCs	Human mesenchymal stem cells
HA	Hyaluronic acid
HAMA	Methacrylated hyaluronan
HA-TA	Hyaluronic acid-tyramine
HE	Heating element
HEPA	High efficiency particulate air
HMW	High molecular weight
HP	Hewlett-Packard
IR	Stereolithography Infrared Stereolithography
ICE	Ionic-covalent entanglement
IPNs	Interpenetrating networks
kDA	Kilo Daltons
kHz	One thousand hertz
LAB	Laser-assisted bioprinter

LED Light-emitting diode
LFS Low force stereolithography
MC Methylcellulose
MRI Magnetic resonance imaging
nHAp Hydroxyapatite nanoparticles
NM Nanometer
PEG Polyethylene glycol
PEGDA Polyethylene glycol diacrylate
PH Potential of hydrogen
RGD Arginyl-glycyl-aspartic acid
SLA Stereo lithograph apparatus
TE Tissue Engineering
UV Ultraviolet
UV-C Germicidal Ultraviolet-C
VdECM Vascular-tissue derived extracellular matrix

CHAPTER 1

The Emerging Role of Biosensors in the Identification, Characterization, and use of Natural Bioactive Compounds

Abhay Dev Tripathi[1,#], **Vivek Kumar Pandey**[2,#], **Soumya Katiyar**[1] and **Abha Mishra**[1,*]

[1] *School of Biochemical Engineering, Indian Institute of Technology (Banaras Hindu University), Varanasi-221005, India*

[2] *Department of Pharmacology and Nutritional Sciences, University of Kentucky, Lexington, Kentucky, USA*

Abstract: High specificity, less reagent requirement, swift response time, and high throughput screening make biosensors popular for detecting disease biomarkers, monitoring diseases, drug discovery, and other ecological applications such as the detection of environmental pollutants. Emerging health disorders demand targeted drugs with lower side effects in terms of advancing towards a low medicinal load. Active ingredients present in the different parts of plants and microorganisms have been used for several medical purposes for ages. Recent research has identified multiple promising natural bioactive compounds possessing the potential to mitigate several life-threatening diseases like Cancer, Diabetes, and Neurological disorders. Identifying such bioactive chemicals in the crude extract from various plant sources like leaves, roots, bark, fruits, and seeds, as well as in microbial extracts, is a tedious work that requires complex instrument setups, lengthy methods, and plenty of time, sometimes many years. The development and use of biosensors for natural bioactive moieties can overcome such problems and expedite the drug discovery process. This chapter provides a summary of the available biosensors for bioactive chemicals detection in extracts and fractions of organisms/plants, their types, design, and methods used for that purpose. Moreover, the chapter highlights the current use and the progress of the development of biosensors for identifying bioactive natural compounds.

Keywords: Biosensors, Cell-free biosensor, Cell-based biosensor, Nano-based biosensor, Phytochemicals.

* **Corresponding author Abha Mishra:** School of Biochemical Engineering, Indian Institute of Technology (Banaras Hindu University), Varanasi-221005, India; E-mail: abham.bce@itbhu.ac.in
# Shared co-first authorship contributed equally to this paper.

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

INTRODUCTION

Natural bioactive compounds are the chemicals produced by plants or the chemicals that are part of the plant's structure and physiology. These bioactive compounds are more commonly referred to as phytonutrients and can be part of the roots, stem, bark, leaves, flowers, and fruits of plants [1]. Bioactive compounds can be beneficial to health as they possess nutritional and medicinal values; on the other hand, they can be toxic and harmful to human health as well [2, 3] Major forms of bioactive compounds are classified as flavonoids, alkaloids, polyphenols, anthocyanins, pigments, vitamins, fatty acids, volatiles, and essential minerals [4]. In the past few decades, phytochemicals have been studied extensively for their medicinal efficacies and are well known for treating/lowering the risks of several diseases like malaria, measles, dysentery, constipation, stomachache, yellow fever, *etc*. Moreover, phytoconstituents are also well documented for their analgesic activities, antimicrobial activities, anti-inflammatory, anti-oxidative activities, anti-hyperglycemic activities, hepatoprotective and reno-protective activities [5– 8]. Recent research shows evidence of bioactive compounds regulating multiple signaling pathways during multiple metabolic disorders like diabetes and cancer [9– 11]. Flavonoids like Morin are reported to modulate insulin signaling, apoptotic pathways, ER stress, and the expression of glucose transporter proteins [7, 8, 12]. Moreover, several polyphenols like epigallocatechin gallate are reported to regulate MAPK kinases, p53, and other proteins involved in the progression of multiple cancers [13]. These examples demonstrate the potential of bioactive compounds to be exploited as therapeutic agents in several incurable diseases. So far, more than 10,000 phytochemicals have been identified, while very few (~150) have been evaluated in depth for their medicinal potential [14]. Moreover, a single plant and/or part of the plant may contain thousands of bioactive compounds, which could be beneficial for nutritional purposes as well as medicinal purposes. Identifying and characterizing these active compounds present in plants are not only complex but time taking too; developing specific biosensors to identify the specific type of the phytochemical may amplify the process. Biosensors can be very useful in the characterization of the bioactive compounds as well and can help in narrowing down the lead molecules out of numerous phytochemicals present in the crude extract.

Biosensors are devices that work based on biochemical reactions and measure the proportions of the analytes present or the end products of that biochemical reaction [15]. Biosensors require several components to work, including biocatalysts (enzymes), bioreceptor, transducers, signal amplifiers, display units, and the analyte that need to be detected [15, 16]. A transducer and a biosensing component are the conventional components of a biosensor. It is utilized for the detection of several components, including contaminants, a specific marker protein, microbial load, metabolites and numerous other compounds. It also has a wide range of uses in the medical field, food industries, and several other industries that demand accurate and reliable tests for screening samples [17]. A perfect example of a commonly used biosensor is Glucometer which is used to measure blood glucose levels.

This chapter explores the use of biosensors in identifying and characterizing phytochemicals which can be useful in drug discovery. The development of compatible and reliable biosensors for selecting bioactive compounds as lead molecules and identifying/isolating toxic plant chemicals can accelerate the speed of drug discovery and disease treatment.

CONSTRUCTING BIOSENSORS FOR DETECTING AND CHARACTERIZING PHYTOCHEMICALS

Development of the specific biosensors depends upon the information regarding the analyte to be detected, such as the chemical nature of the analyte, the concentration of the analyte, intermediated products, interfering species, and the type of matrix [18]. Identifying an end or intermediate product of the biochemical reaction that can be detected by the sensor of the biosensor is an important and tedious process in the development of biosensors for detecting bioactive plant chemicals [19]. Choosing a biosensor also depends upon the nature of the reaction and/or the type of sensors used to construct it. Below is the list of a few types of sensors or detectors used in developing biosensors:

Electrochemical sensors: These sensors are majorly based on the enzymatic catalysis that consumes or liberates electrons that can be captured by the sensors. Electrochemical sensors can be further classified into four types of sensors [20–22]:

a. *Amperometric Biosensors* (detect electrical current while keeping potential constant)
b. *Potentiometric Biosensors* (detect electrical potential)
c. *Impedimetric Biosensors* (detect electrical impedance)
d. *Voltammetric Biosensors* (detect current when applied to a specific voltage)

Immunosensors work based on the specificity of antibodies to their specific antigens.

Nucleic Acid biosensors work based on the interaction properties of DNA and RNAs to their complementary strands.

CHAPTER 2

Role of Wearable Biosensors in Healthcare

Himani Yadav[1], **Bhaskar Sharma**[2], **Ravi Kumar Goswami**[3], **Avanish Kumar Shrivastav**[4], **Vivek K. Chaturvedi**[5], **Prem L. Uniyal**[1] and **Priti Giri**[1,*]

[1] *Department of Botany, University of Delhi, Delhi-110007, India*

[2] *Neurobiology Laboratory, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, 110029, India*

[3] *Department of Zoology, Hindu College, University of Delhi, New Delhi-110007, India*

[4] *Department of Biotechnology, Delhi Technological University, Delhi110042, India*

[5] *Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India*

Abstract: These days, wearable biosensors are a very valuable tool for tracking the start of various acute and chronic diseases. Wearable biosensors (WBSs) are small, electrical devices that coordinate and collect sensations into the human body and can be present in the form of tattoos, gloves, clothing and inserts. WBSs are a flexible and practical tool for use in the healthcare industry, thanks to their ability to detect information, record it and estimate it accurately. WBSs help patients and doctors to communicate in both directions. It is simple to do painless evaluations of bodily fluids using various biochemical markers such as spit, sweat, skin, and tears. As the continuous state of capabilities of wearable and adaptable sensors continues to advance, the creation of new wearable gadgets that can fill the gap and handle the advantage of human well-being checking and clinical application is advancing. Blood is still the most crucial bio-liquid for assessing a person's health, even though more attention has been paid to other bodily fluids that are naturally secreted and severe functions that are similar to those of blood. There has been a lot of interest in the capacity of compact biosensing devices to identify the analyte in bio-liquids for the early detection of human well-being.

Keywords: Biomarkers, Gadgets, Healthcare, Wearable biosensors.

* **Corresponding author Priti Giri:** Department of Botany, University of Delhi, Delhi-110007, India; E-mail: giripriti06@gmail.com

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

INTRODUCTION

These days, the advancement and customization of wearable biosensors make them a very useful asset for monitoring the onset of various acute and chronic diseases. Wearable biosensors (WBSs) are compact electronic gadgets that coordinate and collect sensations into the human body and can be present in the form of tattoos, gloves, clothing and inserts. Detection of information, recording, and accurate estimation makes WBSs a versatile and convenient gadget for utilization in healthcare. Two-way communication is facilitated by WBSs among patients and doctors. Painless evaluation of human body liquids *via* different biochemical markers like spit, sweat, skin, and tears can achieve easily. With the development and coordinated application of material science, mechanical designing and advancements in remote correspondence, different wearable gadgets have been created and utilized for examining biomarkers to deliver appropriate medical care. With a maturing populace, the proof of sanitation and illness episodes has expanded. With the innovation and usability of WBSs, its market can ascend to USD 70 billion by 2025 [1].

A normal biosensor has two essential useful units, *i.e.*, a "biorecognition component or bioreceptor" (protein, immunizer, DNA, nucleic corrosive, peptide, and so on) and a physicochemical transducer, for example, piezoelectric, temperature, optical and electrochemical. The transducer is responsible for the change of a biorecognition occasion into quantifiable units, and the bioreceptor is liable for perceiving the objective analyte specifically. These gadgets were initially created and planned for single-use estimations, for instance, glucometer, glucose test strips, and glucowatch. Besides, the advancement in biosensors has prepared them for harmless checking in medical care and biomedical applications [2, 3].

WBSs can be ordered into biophysical sensors, movement state and biochemical sensors as per the various demands of the consumer. The movement sensors are utilized mainly to gauge actual human boundaries, for example, walking, rest, tremor and an assortment of long-haul data [4, 5]. With coordinated lab-on-chip innovation, researchers and lab labourers can exactly gauge biomarkers in organic liquids to screen for ailments and digestion [6 - 8]. Wearable biophysical sensors enchanted qualities to contact with skin to give an ongoing estimation of biophysical boundaries, for example, pulse and temperature, which have a huge breakthrough in medical care applications. The biophysical and movement state sensors are accessible and broadly utilized by buyers.

Among different types of biosensors, electrochemical-based sensors have shown maximum benefits because of their awareness, fast reaction, simplicity of development, and capacity to work with low utilization of force. Cathode detection plays an important part in the constitution of wearable sensors as detecting anodes also requires an innovative metal-based film cathode. Different headways have been accounted for by looking at new materials, such as the mixture of metallic nanoparticles, nanocomposite, carbon, and polymeric materials. Advancement in the miniature assembling of biosensors helps in improving the working boundaries of the detecting anodes [9]. Lately, huge endeavours have been made to achieve such sort of wearable sensors to perceive the different biomarkers that influence well-being. Finally, future viewpoints and difficulties are likewise examined for the enhancement WBSs in healthcare [10, 11].

WEARABLE DEVICES BASED ON DESIGN OR UTILITY

Customization of wearable biosensors in the administration of well-being has acquired huge consideration starting in the 21st century. Wearable gadgets can be named as per different wearable groups like wearable materials (socks, shirts and shoes), wearable gears (caps and glasses), and tactile gadgets (gloves and watches) for the assessment of well-being. With the coordinated scaled-down gadgets and headways in advances (microelectronics and remote correspondence), wearable biochemical sensors have profoundly implanted and turned into a vital piece of our lives [12 - 14].

Wrist-Mounted Wearable

Wearable Devices (WDs) are normally worn on the wrist. WDs are created with long battery life for checking the change in physiological boundaries to assess the crude signs into constant interpretable information. Earlier, wrist-mounted wearables were essentially accelerometer-based ones, for example, smartwatches, but nowadays, it has incorporated biometric detecting, *i.e*., pedometer. Wristbands or smartwatches are utilized as harmless gadgets for monitoring human health [15].

Wristbands

Though watches and wristbands show resemblance, wristbands are famously sorted as wrist-worn wearable gadgets and are explicitly intended to follow human well-being. For instance, Jawbone made the UP4 band, which chips away at bio-impedance sensors to screen exercises, that is, strolling and following the capacity to record the dozing cycle. It similarly can catch signals, such as pulse, internal heat level, and galvanic skin reaction (GSR), utilizing different sensors (bio-impedance, tri-axis) situated on the inward side of the band. In any case, UP4 does not have a screen show, and the information can be perused through the cell

CHAPTER 3

3D Bioprinting of Advanced Bioinks for Tissue Regeneration and Biosensor Development

Alma Tamunonengiofori Banigo[1,*] and **Chinedu Chamberlin Obasi**[2]

[1] *Department of Developmental Bio Engineering, Faculty of Science and Technology and TechMed Centre, University of Twente. Drienerlolaan 5, 7522 NB Enschede, The Netherlands*

[2] *Department of Pharmaceutical Biotechnology, Institute of Pharmacy, Martin Luther University, Halle-Wittenberg, Germany*

Abstract: Three-dimensional (3D) bioprinting technology has become a unique system for tissue regeneration and biosensor development by controlled deposition of bioinks to produce complex constructs. Different bioprinters including laser-assisted and extrusion-based have been introduced and used to produce constructs with high resolution, cell viability and shape fidelity for tissue development. In addition, microfluidic technology, organ-on-a-chip and electrospinning technology are used to produce biosensing products to diagnose and monitor living systems. One of the most critical materials used for bioprinting is bioink. Several bioinks of an advanced level and different compositions have been developed too. Here, we briefly highlighted the characteristics, advantages, and disadvantages of some bioprinters and advanced bioinks that have been developed recently. We also stated some tissue engineering applications with the use of 3D bioprinting. Lastly, we mentioned a few key areas for main focus in the future.

Keywords: Applications, Advanced boinks, Bioprinting, Hydrogel, Tissue regeneration, Tissue engineering.

INTRODUCTION

Worn-out or damaged living tissues occur as a common phenomenon in humans. The ability to repair or regenerate these tissues that are damaged from diseases is termed tissue regeneration [1]. The conventional techniques employed for tissue regeneration depend on the transplantation of tissues. Unfortunately, transplantation cannot be initiated in this case without the presence of a donor, which could be scarce and may bring about the risk of graft rejection due to an immune response.

* **Corresponding author Alma Tamunonengiofori Banigo:** Department of Developmental Bio Engineering, Faculty of Science and Technology and TechMed Centre, University of Twente. Drienerlolaan 5, 7522 NB Enschede, The Netherlands; E-mail: a.tamunonengioforibanigo@utwente.nl

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

Tissue engineering (TE) is a branch of biomedical engineering (BME) that focuses on tackling these challenges of tissue regeneration [2]. Specifically, additive manufacturing (AM) is a technique in TE that has the principles of some fields, including biology and material science [3, 4], that can perform the following functions:-

1) To produce novel tissues for restoring damaged ones;

2) To mimic the native complexity of the cell micro-environment;

3) To facilitate cellular activities, including differentiation, proliferation, and tissue regeneration [5].

The conventional methods lack the 3D cell distribution [6], take time, are less efficient [5], and many more [5, 7]. AM enables the construction of complex tissues based on a top-down approach by using precise and accurate computer-generated 3D tissue models [8].

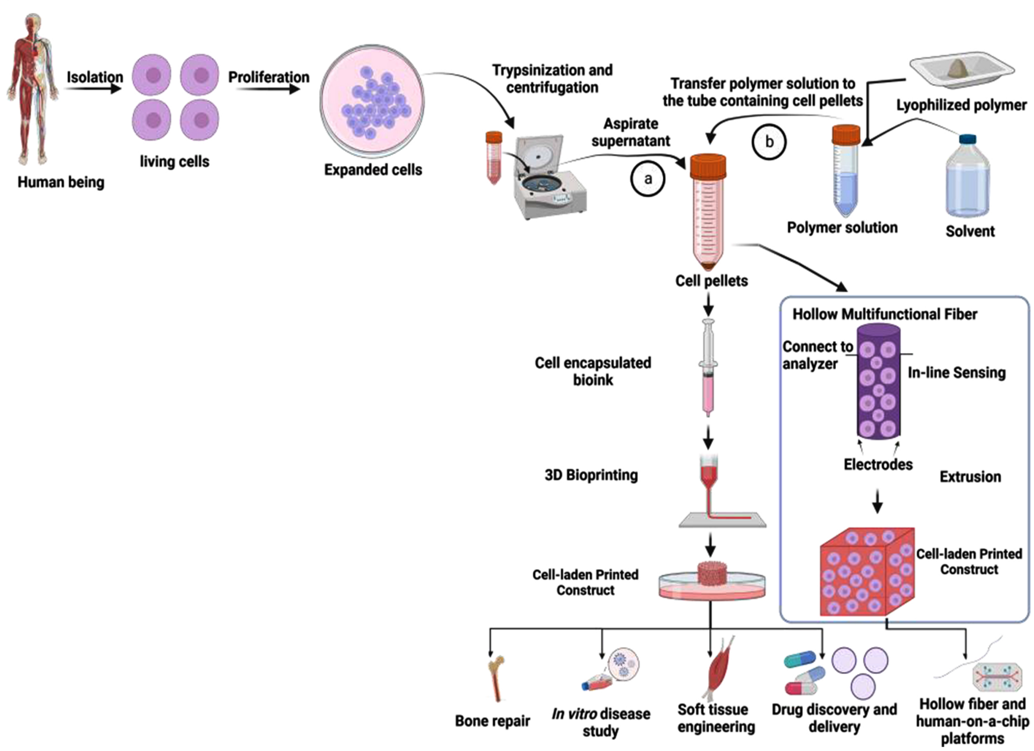
3D bioprinting is a branch of AM [5] that has been expanding rapidly and currently, focuses on producing biomimetic tissue-like constructs. This technology utilizes some imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), to make a computer-aided design (CAD) [9]. The design is used for layer-by-layer (bottom-up approach) deposition of biomaterials, viable cells, and other supporting materials (including growth factors, and nucleic acids) into accurate and precise geometries onto a substrate [10], and they are positioned precisely with functional components to fabricate tissue-like 3D structures [11] or constructs with unique structure and function [9, 11]. Based on the presence of cells, tissues, and other living components, observations such as viability, the biocompatibility of the present materials, cell sensitivity to the printing techniques, perfusion, toxicity and many more have to be considered [5, 12]. These bioprinted tissues with enhanced properties and intercellular communication could help in modeling the human *in vivo* physiology [5]. Hence, the outcome can be used in pre-clinical trials as animal models lack the ability to detect human pathophysiological responses [13]. The models from the expansion of 3D bioprinting technology can be used for different applications, including:-

- *In situ* surgical cartilage repair [14]
- *In vitro* disease modeling [9]
- Drug screening, disease mechanism research, and pre-clinical studies in tissues of interest [15 - 24]

- *In situ* wound dressing [25]
- Biosensor development [26 - 28]

For the latter aspect ‘biosensor development’, 3D bioprinting technologies are being employed to develop biosensing platforms including impedimetric-based sensing platforms to monitor both conditions of living cells (proliferation and activity in either suspensions or adherent cultures) and bioink (composition and quality) during continuous micro extrusion [27, 29]. In comparison with traditional 3D printing to produce cell-free scaffolds, 3D bioprinting needs several technical requirements and approaches to fabricate 3D constructs with both biological and mechanical properties for functional tissue restoration and biosensor development. The 3D bioprinting process, some advantages of 3D bioprinting over traditional 3D printing, and several approaches to 3D bioprinting have been outlined in Figs. (**1a, b and c**), respectively.

a)



(Fig. 1) contd.....

CHAPTER 4

Biosensors for Neurodegenerative Diseases

Gaurav Mishra[1,*], Anand Maurya[1], Anurag Kumar Singh[2], Marjan Talebi[3], Rajendra Awasthi[4] and **Manmath Kumar Nandi[1]**

[1] *Institute of Medical Sciences, Faculty of Ayurveda, Department of Medicinal Chemistry, Banaras Hindu University, Varanasi, 221005, Uttar Pradesh, India*

[2] *Centre of Experimental Medicine & Surgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, Uttar Pradesh, India*

[3] *Department of Pharmacognosy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[4] *Department of Pharmaceutical Sciences, School of Health Sciences and Technology, University of Petroleum and Energy Studies (UPES), Energy Acres, Bidholi, Via-Prem Nagar, Dehradun – 248 007, Uttarakhand, India*

Abstract: Since the conception of biosensor technology in biomedical research, this field is emerging as a promising and high-throughput tool for neuro-engineering and neurosciences research. It has been postulated that the accumulating property proteins are the basic cause of neurodegenerative diseases, such as Parkinson's disease, Alzheimer's disease and prion diseases. Thus, neurodegenerative diseases are also called "protein misfolding disorders". Biosensors have a wide range of applications in biomedical research, including optical and electrochemical detection of biometal-protein interactions, detection of biomarkers, such as β-amyloids, apolipoprotein, and tau proteins, and microRNA in blood and cerebrospinal fluid in neurodegenerative diseases. These are composed of primary biological recognition elements that convert the chemical signal into the voltage or current that evaluates the physical signal by preparing a plot of sensor response against the analyte concentration. This chapter presents a bird's eye view on various aspects of progress in biosensor development with special emphasis on their application, including metal-protein interactions studies, detection of neurotransmitters using aptamers and calixarenes, detection of biomarkers proteins, such as α-synuclein for Parkinson's disease, apolipoprotein, tau and β-amyloid proteins for Alzheimer's disease, and prion proteins. The chapter also summarizes the novel materials reported for improved biosensor performance. This chapter will be of high relevance to the biological scientists working in neuro-engineering and neurosciences research.

[*] **Corresponding Author Gaurav Mishra**: Institute of Medical Sciences, Faculty of Ayurveda, Department of Medicinal Chemistry, Banaras Hindu University, Varanasi, 221005, Uttar Pradesh, India; Email: vatsgaurav880@gmail.com

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

Keywords: Alzheimer's disease, Biomarker, Biosensors, Neuro-biosensors, Neurodegenerative diseases, Nanomaterials, Neurocognitive disorders, Nanotechnology, Parkinson's disease.

BACKGROUND

Early diagnosis of neurodegeneration-focused illnesses that worsen with advancing age is essential because they have an impact on the patient's quality of life and medication. Two well-known examples of neurodegeneration in Parkinson's and Alzheimer's are characterized by dementia and nerve cell death. The identification of biomarkers-recognizable substances in bodily fluids involved in the onset or development of neurodegenerative manifestations could make an early diagnosis of neurodegenerative, demyelinating illnesses and autism spectrum disorder possible.

In order to more accurately identify potential biomarkers of the neurodegenerative process and explore the disease's state prognosis, research on biosensors has increased with the objective to identify the target analyte having maximum specificity. This book chapter aims to give a summary of the neuro-biosensors developed based on biomarkers found in body fluids for the identification and management of illnesses regarding the degeneration of neurons with preference to most common Parkinson's disease (PD) and Alzheimer's disease (AD), as well as a summary of the neurodegeneration pathway, which may be directly linked to early diagnosis of the disease. It is an urgent requirement for the treatment. Practically, neuro-biosensing technologies make a connection between various scientific disciplines, such as neuroscience, pharmacology, nanotechnology, electrochemistry, photometry and electronics.

Over the past decades, biosensors identified by using optical and electrochemical technologies, are at the forefront because of developments in material science, such as aptasensors, exosomes, nanomaterials, and wearable biosensors. In the current study, the most recent advances in biosensors used for the detection of neurodegeneration based on optical and electrochemical techniques are evaluated in all aspects.

INTRODUCTION

Neurodegenerative disorders (NDDs), also known as “protein misfolding disorders,” are among the most life-limiting diseases associated with significant deficits and impairments among the many age-related ailments that people experience [1].

Neuronal death is caused by various reasons, including excitotoxicity, mitochondrial malfunction, and extracellular buildup of dangerous chemicals. This may affect both physical and mental functioning [2]. Thus, the prognosis of the disease's progress or the effectiveness of the treatment may be crucial for enhancing the quality of life of the affected person.

Sophisticated neuro-biosensing technologies have been developed as a result of the identification of biomarkers in biofluids for the detection of neurodegenerative illnesses, such as Alzheimer's disease (AD) (a later life disease occurrence, categorized as the most common type of dementia), Parkinson's disease (PD) (a demyelinating disorder that affects a body part having the inability to move, as seen in multiple sclerosis (MS) [3, 4], prion diseases, and Huntington's disease (HD) [5]. The need for early diagnosis is also emphasized in the whole pathophysiology of the neurodegenerative pathway [6].

Applications for neuro-biosensors mainly center on the detection of amyloid-beta peptides [7], tau proteins, reactive oxygen species (ROS), lactoferrin, acetylcholine [8], miRNAs [9], transition metals [10], epigenetics, and apolipoprotein in AD [11, 12], dopamine, urate, ascorbic acid, 8-hydroxy-2′ -deoxyguanosine, apolipoproteins (A1 and E), DJ-1, and alpha-synuclein in PD [13], immune cells and inflammatory markers in Amyotrophic lateral sclerosis (ALS) [14], a protein in human HD (huntingtin) and in prion diseases (prion) and also demyelinating disorders, such as MS [15, 16].

Despite having a lengthy history, bioanalytical approaches have just achieved an important milestone. Biosensors are examples of analytical machinery that transform biological reactions into quantitative signals. To locate or assist in diagnosing NDDs biomarkers and also autism spectrum disorder (ASD) [17], biosensors offer a sensitive, targeted, specific, and reasonably priced option [14, 18]. Biosensors are used to advance drug development, observe an illness, and detect several substances, including disease-causing biomarkers [19].

APPLICATIONS OF BIOSENSORS IN NEURODEGENERATIVE DISEASES

The recognition layer of a biosensor is made up of biological components that connect with the targeted analyzers, such as nucleic acids (DNA & RNA), peptides, antibodies, antigens and enzymes [20]. Additionally, unique bio-sample based technologies will be used in biosensors with sizes ranging from micro to femto, including biosensors based on various biofluids such as Cerebrospinal fluid (CSF), urine, blood, tear, and saliva [21]. Biosensors can be classified into different groups on the basis of signal types they receive, including optical, electrochemical, plasmonic, thermometric, field-effect transistor-based sensor

CHAPTER 5

Biosensors for Protein Bio-Sensing and Detection of Bacteria and Viruses

Himani Yadav[1], **Bhaskar Sharma**[2], **Priti Giri**[1], **Avanish Kumar Shrivastav**[3], **Vivek Kumar Chaturvedi**[4], **Prem L. Uniyal**[1] and **Ravi Kumar Goswami**[5,*]

[1] *Department of Botany, University of Delhi, Delhi-110007, India*

[2] *Neurobiology Laboratory, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, 110029, India*

[3] *Department of Biotechnology, Delhi Technological University, Delhi-110042, India*

[4] *Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India*

[5] *Department of Zoology, Hindu College, University of Delhi, New Delhi-110007, India*

Abstract: The concept of a biosensor was first proposed in 1962 by Clark and Lyons, who developed an oxidase enzyme electrode for the detection of glucose. Since then, the development of nanotechnology has prompted biosensors to evolve and become more specialized for a variety of applications. Currently, at the forefront of science, bio-sensing applications combined with nanotechnology have implications for multiple fields, including medicine, biology, environment, drug delivery, and food safety. In recent decades, bacterial and viral diseases have seriously threatened human safety. Prioritizing the rapid detection of outbreaks, which pose a major threat to the healthcare system and could have a catastrophic socioeconomic impact, will help stop them. Scientists are conducting extensive research to develop sensitive diagnostic techniques and effective medicines.

Keywords: Biosensors, Bacteria, Diagnosis, Nanotechnology, Viruses.

INTRODUCTION

The idea of a biosensor was initially brought up by Clark and Lyons in 1962 when they created an oxidase enzyme electrode for the detection of glucose [1]. Since then, the growth of nanotechnology has encouraged the evolution and specialisation of biosensors for various applications [2]. Nanotechnology is currently at the cutting edge of science, and its combination with bio-sensing

* **Corresponding author Ravi Kumar Goswami:** Department of Zoology, Hindu College, University of Delhi, New Delhi- 10007, India; Email: ravigoswamigen@gmail.com

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

applications affects a variety of sectors, including medicine, biology, the environment, drug delivery, and food safety [3].

However, considering the importance of bacterial and viral diseases in human health today, the detection of pathogens has emerged as one of the most important goals for these devices. The reverse transcription polymerase chain reaction (RT-PCR), the gold standard for pathogen identification, is widely used to detect viruses and bacteria. As part of standard detection methods, these pathogens typically must be isolated, cultured, and subjected to biochemical testing. In addition, serological tests such as ELISA are used to detect antibodies and immunoglobulins, which are essential for identification [4]. However, some of these methods are labour intensive and often take a long time to produce results.

Although there are numerous techniques for locating viral particles, their practical application is limited by several difficulties. These restrictions consist of:

1. Less precise and sensitive

2. The requirement for sample cleaning and preparation

3. It takes time

4. Increased instrument, accessory, and upkeep costs

5. Widespread accessibility

6. The instruments' intricate operation

7. The need for highly qualified technical staff

8. Insufficient for quick, on-site analysis

In light of viruses' adaptability and potential reproduction sites, there is a need for more advanced, more efficient methods for the rapid detection of viral analytes. These approaches must ensure greater accuracy, portability, ease of use, and widespread accessibility for testing the general population. As a result, novel strategies based on nanotechnological developments have arisen as viable and simple solutions for quickly and effectively identifying infections. On the one hand, nanoparticles (NPs) have proven to have exceptional anti-pathogen characteristics and have been exploited to create novel devices and solutions that help with this public health concern [5]. Since zoonosis is a real concern, the focus extends beyond human illnesses to include those affecting animals. Gold nanoparticles (AuNPs) and quantum dots (QDs) were used to create an optical biosensor for the detection of the porcine reproductive and respiratory disease virus [6]. On the other hand, there is a growing interest among scientists worldwide in using DNA biosensors or sequence-specific DNA detectors for clinical studies. A combination DNA-based piezoelectric biosensor was created for the simultaneous detection and genotyping of high-risk human papillomavirus (HPV) strains [7].

These gadgets are useful *(e.g*., they allow point-of-care (POC) testing using a nano-biosensor built into a smartphone), quick, and are regarded as novel technologies that offer an alternative solution to the drawbacks of conventional detection methods that have been stated [8]. These technologies have been used to investigate bacteria like *Escherichia coli* and *Salmonella spp.* as well as viruses like the Ebola virus, human immunodeficiency virus (HIV), and more recently, acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that affect human health [9]. Biosensors are analyte detection devices that combine a biological component with a physicochemical detector known as a biosensor [10]. The biosensor's design and intended use affect how an analyte is detected. With the addition of simple accessories, several everyday items, like cell phones, can be utilised as biosensors, where they built a non-invasive smartphone-based urea biosensor using saliva as a sample [11]. This enables quick and affordable preliminary detection [12]. Typically, biosensors identify substances linked to disease, including nucleic acids, proteins, and cells. The physiologically sensitive element, the detector element, and the reader device are their three main constituents, which allow for this. The biomolecules are identified using nucleic acids, organelles, antibodies, enzymes, and microbes. Researchers also need to determine the prerequisites for obtaining a functional gadget per the desired usage.

Therefore, multidisciplinary research is essential to choosing the right material, transducing technology, and biological components before putting the biosensor together [13]. Biosensors are used in the clinical setting to find biomolecules linked to disease. These tools are capable of detecting biochemical disease indicators in bodily fluids, including saliva, blood, or urine. A non-invasive glucose testing technique is based on a dispensed saliva nano-biosensor to increase patient compliance, lessen complications, and lower expenses associated with managing diabetes. In comparison to the UV spectrophotometer, they achieved exceptional accuracy outcomes in the clinical testing. The disposable gadget can therefore be suggested as an option for tracking salivary glucose in real-time [14]. Numerous more clinical diagnostic uses for biosensors exist, including cholesterol, cardiovascular disease markers, cancer or tumour biomarkers, allergic reactions, and infections with pathogenic bacteria, viruses, and fungi. In addition, biosensors can be used to detect bacteria and viruses in water and food, which are potential disease-causing agents. For the quick *in-situ*

CHAPTER 6

Biosensor: A Technology that Changed the way of Diabetes Diagnosis

Sushil Kumar Dubey[1,*], Bhaskar Sharma[2], Divya Mishra[3] and **M.P. Singh[1]**

[1] *Centre of Biotechnology, University of Allahabad., Prayagraj, Uttar Pradesh, 211002, India*

[2] *Neurobiology Laboratory, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, 110049, India*

[3] *Centre of Bioinformatics, University of Allahabad, Prayagraj, Uttar Pradesh, 211002, India*

Abstract: Over the past few decades, technology has greatly improved, with more accuracy and efficiency in monitoring the blood glucose level of diabetic patients. To monitor the blood glucose level, several glucose biosensors have been developed. However, the accuracy, efficiency, standardization and training of the users in an easy way is still a challenge. Biosensors are a non-invasive method that helps medical workers to find the required doses of insulin for diabetic patients. In this chapter, we will discuss different types of biosensors developed, their working mechanism, and the current scenario of biosensors in diabetes diagnosis.

Keywords: Biosensors, Diabetes, Glucose Biosensors, Mechanism.

INTRODUCTION

Diabetes is a serious and complex health problem in the 21st century. Globally, there will be 422 million people with diabetes as of 2014, many of whom live in low- and middle-income countries. The number of people with diabetes has been steadily increasing over the decade. It also has been estimated to affect 552 million people around the globe by 2030 [1]. Diabetes is a major cause of other severe diseases, including heart and kidney disease, and can also cause blindness in the elderly, yet almost half of the diabetes-related cases remain undiagnosed. Diabetes is one of the leading causes of death worldwide, having 1.6 million death per year, and its research has never been more significant [2]. To reduce the number of deaths caused by diabetes, the WHO has listed the priority medical devices to manage cardiovascular diseases and diabetes (**released on 30 June 2021**), which will help healthcare providers and policymakers prioritize the procurement of medical devices for diabetic patients. The list consists of hundreds

* **Corresponding author Sushil Kumar Dubey:** Centre of Biotechnology, University of Allahabad, Prayagraj, Uttar Pradesh–211002 India; Email: sushildubey40@gmail.com

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

of medical devices that are mainly required for the detection and treatment of diabetes. It starts from primary care facilities to extremely specialized hospitals and medical devices that are needed for health-related emergencies (such as hypo or hyperglycemic emergencies, WHO 2021).

According to the reports suggested by Diabetes Australia, around 12% of global health costs are spent on diabetes, which is USD 673 billion [2]. Therefore, it is significant to focus on effective diagnostic tools and low-cost monitoring devices for diabetes. There are mainly three types of diabetes: type 1, type 2 and gestational diabetes. Therefore, type 1 diabetes mellitus is a chronic metabolic disorder that is characterized by high fasting glucose, in which beta cells (from islets of Langerhans in the pancreas) can no longer provide insulin. Insulin is needed to maintain the level of blood glucose in the range of 4.0-5.5 mmol/L [3]. Likewise, it is suggested that when the body fails to maintain the optimum range of blood glucose, it leads to hypo or hyperglycaemia. The condition of hypo or hyperglycaemia will further lead to physiological complications and provide severe damage to major organs. In the case of an undiagnosed diabetic patient, the type 1 diabetes symptoms include polydipsia (thirst), polyuria (excessive urination), weight loss, constant hunger, and fatigue, among others [4]. According to research, type 1 diabetes cannot be preventable at this time, but its monitoring is of utmost significance for diabetic patients. Type 2 diabetes is the result of the degeneration or lack of insulin response. However, type 2 diabetes is the most common type of diabetes in the world today, representing 85 to 90% of all cases [1]. Type 1 diabetes is more readily managed with regular diet, exercise, and the control of lipids and blood pressure [4], although insulin can still be needed. However, further prevention from developing type 2 diabetes will significantly decrease the risk of complications, *i.e.*, blindness, kidney failure, and cardiovascular disease. Evidence suggests that type 2 diabetes can be cured through accurate management of dysregulated insulin and glucose [5]. Hence, real-time glucose measurement is significant for preventing and predicting glucose levels and following medications to manage diabetes. Certainly, gestational diabetes mainly occurs during the period of pregnancy, affecting between 12 and 14% of pregnant women. Most gestational pregnancies are healthy pregnancies and produce healthy offspring if they follow good eating habits, and most women will no longer have high blood sugar after the baby is born [1]. Thus, close glucose level measurements are highly recommended by healthcare specialists to guide proper exercise and healthy food for pregnant women. Currently, the most popular and significant approach for diabetes management is focused on at-home glucose monitoring using the finger-pricking method. In the finger pricking method, the patients must maintain their daytime sugar levels between 4.4 and 6.7 mm/L, using a glucose meter. Although this measurement approach can become a burden, that relies on a high frequency of glucose monitoring to result in good glycaemic control [6], and it doesn't warn of the occurrences of hypoglycaemia. While testing, the wounds will cause through needle sticks which contain the risk of infection. In the case of children patients, the pain may cause fear, avoid blood glucose monitoring, and they can refuse medical treatment. Also, this approach can lead to loss of fingertips sensations with the occurrence of pain [3]. The finger-pricking testing is also known to serve unreliable data because of inaccurate blood sampling and lead to infections due to regular intrusive testing.

An alternative approach is the non-intrusive continuous glucose testing approach that provides a comprehensive insight into the patient's glucose monitoring and refuses medical treatment. However, research has been done to compare continuous glucose monitoring with or without regular blood glucose measurements and confirmed that it is as efficient and safe to use in adults with type 1 diabetes with a low risk of hypoglycaemia [7].

Evidence suggests that by using continuous glucose monitoring (CGM), patients can essentially reduce their HbA1c levels as opposed to routine care. In addition, CGM medical devices provide better glucose control and reduce the frequency of insulin management; also, more analyses are required to confirm this. With the emergence of chemistry, materials science, computer science, and wearable and wireless technology has made an essential advancement in digital quantifications of our daily routine, respectively. It needed a flexible substrate, an efficient sensor, and a reliable signal report system [8]. The current pandemic situations aid the market demand for disease testing, prevention, and management devices. It also leads the production of wearable sensing devices, which further alleviate an emerging field of research and matching proudly forward from measuring physical activity to health conditions [9]. Wearables have a wide range of uses in healthcare due to their point-of-care nature and non-invasiveness. Wearable medical devices can offer a platform for regular monitoring and recording of physiological information in the form of a device, which can be utilized for tracking patients' current medical situations, diagnoses, and treatment. However, the most common wearable sensor device is a smartwatch that can track regular activities and physiological parameters like temperature, heart rate, as well as sleep cycles. Likewise, wearable devices can also be utilized in the telehealth context that can efficiently measure patients, predict diseases as well as remind wearers to attend appointments by measuring the chemical information, that is, glucose and metal ions, and oxygen levels in our body fluids. This chapter summarises recent ongoing research activities based on the different biosensors for regular glucose measurements over the last 5 years.

CHAPTER 7

Role of Paper-based Biosensor in Diagnostics

Sujeet Singh[1], **Praveen Rai**[2], **Hemant Arya**[1] and **Vivek K. Chaturvedi**[3,*]

[1] *Department of Biotechnology, Central University of Rajasthan, Ajmer, Rajasthan 305817, India*

[2] *National Institute of Plant Genome Research, New Delhi, India*

[3] *Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India*

Abstract: New diagnostic technologies are paper-based sensors that are multifunctional, highly flexible, absorbent, and environmentally friendly. The substrate can be used to design a cost-effective framework for disease detection, prognosis, and surveillance of illnesses that is easy, reliable, and quick in our medical healthcare sector. Paper-based devices are an extremely cheap innovation for fabricating simplified and movable diagnosing processes that can be extremely useful in resource-constrained settings like developing countries, where fully equipped infrastructure and highly skilled medical persons are unavailable. Point-of-care (POC) devices give a significant advantage over traditional procedures for *in-situ* measurement of illness or disease biomarkers, assisting physicians in making decisions. Paper-based analytical devices that combine paper substrates have become popular point-of-need diagnostics over the last decade. We discuss in this chapter the paper-based analytical biosensors and the classification of paper-based biosensors (PBBs) as Dipstick tests, lateral flow assay (LFAs), microfluidic biosensors, and biosensor devices (transducers and biorecognition elements). Furthermore, paper-based biosensors are used to detect malaria and other diseases.

Keywords: Biomarker, Biosensor, Diagnosis, Fabrication, Malaria, Paper, Printing.

INTRODUCTION

Leland C. Clerk discovered the first biosensor in 1956 to detect oxygen [1]. These analytical devices measure the concentration of analytes [2]. For example, in measuring sugar levels in diabetes patients, we use a glucometer, a type of biosensor. There are various types of biomolecules present inside the human cell. The biosensors detect the concentration of a specific biomolecule and analyze human health issues (Fig. **1**). The biosensor is a compact device that helps to

* **Corresponding author Vivek K. Chaturvedi:** Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India; E-mail: vkchaturvedi.nbt@gmail.com

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

determine human health and disease conditions, and the measured biomolecules are called biomarkers [1].

The blood, urine, saliva, and sweat samples were taken from the human body for continuous measurement through biosensor devices. With the help of biosensor devices, patients and doctors immediately get the correct information. It also reduces unnecessary hospital visits and promotes self-management of health and diseases [1]. There are different biosensors, like DNA-based biosensors, piezoelectric biosensors, enzyme-based biosensors, tissue-based biosensors, thermal-based biosensors, and paper-based biosensors.

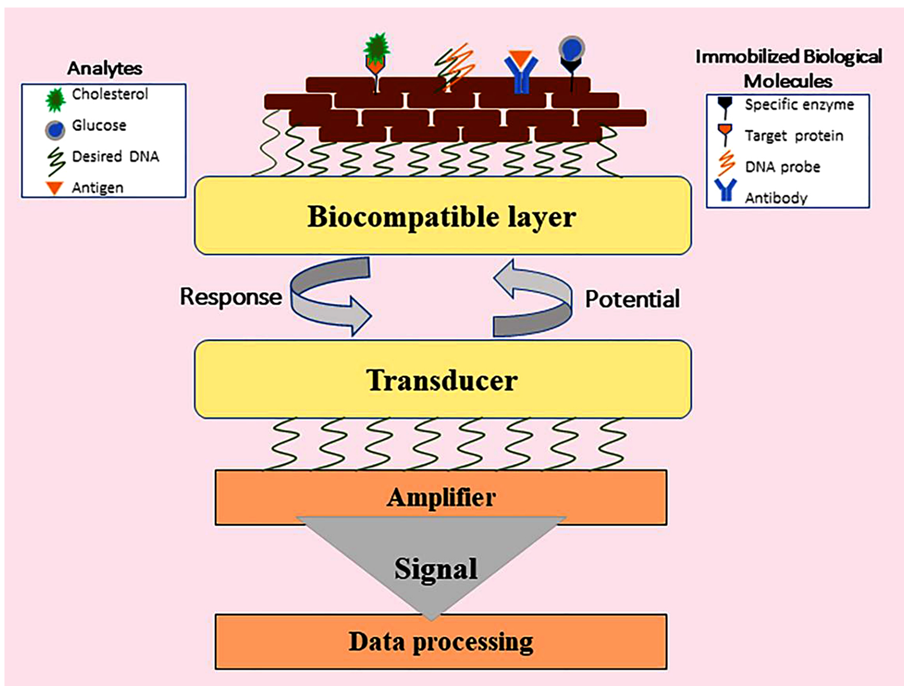


Fig. (1). Working principle of biosensors.

Paper-based Biosensors

To ensure adequate human healthcare, we want rapid, simple, accurate, and low-cost detection methods that can immediately identify the onset of human diseases by using the disease biomarkers in body fluids (serum, blood, urine, saliva, and sweat). Similarly, traditional ELISA (enzyme-linked immunosorbent assay) and spectrophotometric techniques are mostly used to quantify environmental contaminants (*e.g.*, heavy metal ions in industrial wastewater effluent). These biosensor devices did not require skilled personnel to perform diagnostic tests and evaluate results in resource-constrained areas. The use of paper-based biosensor devices comprises the detection of diseases, examining human health conditions, detecting of any biological pathogens, and detecting water and food quality (Fig. **2**). The traditional method for detecting any disease takes a long time and requires a sophisticated device. Still, with the help of point-of-care (POC) devices, it has opened a wide range of diagnoses for *in-situ* analyses. The paper-based biosensor devices have many advantages. The paper-based biosensor is highly flexible, eco-friendly, polymeric, cost-efficient, hugely available, less weighted, and hydrophilic. Due to the porous nature of the paper, the liquid solution flows *via* capillary action, and no external pump is required. In the sample, detecting the analyte due to its chemical reaction can cause a color change, electrochemical properties, and light emission or absorption [3]. The most common detection method depends on the colorimetric changes. The evaluation of the result is to identify the color product generated due to the binding of ligand-analyte, which scanners, cameras, or mobile phones can further quantify. The use of paper-based biosensors has many advantages. (i) it provides a high surface-to-volume ratio; (ii) compatibility with the biological samples; (iii) capillary action; (iv) adsorption properties; and (v) immobilization of antibodies and proteins. The incineration of paper-based biosensors is easy and quickly accessible globally [4]. After all, fabrication techniques for paper-based microfluidic devices, such as wax printing, are very cheap.

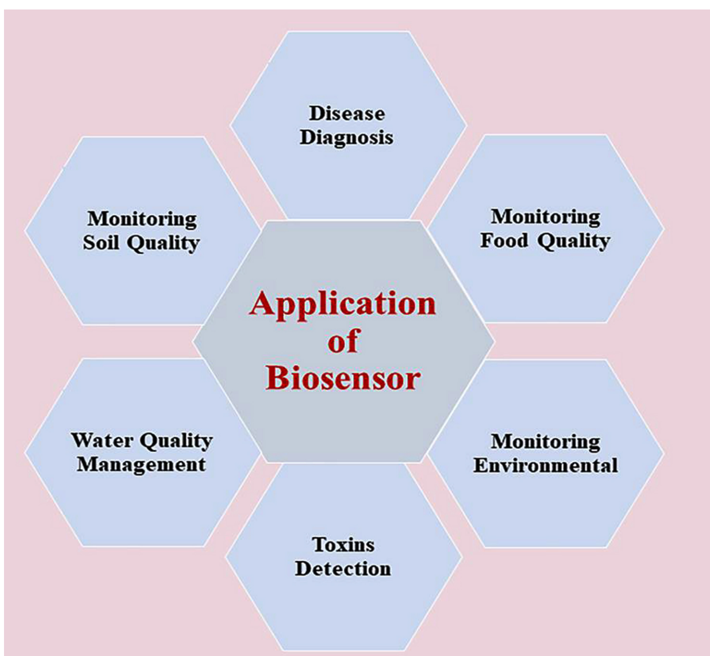


Fig. (2). Application of biosensors.

CHAPTER 8

Enzymatic Biosensors and their Important Applications

Mridula Chaturvedi[1,*]

[1] *Amity Institute of Biotechnology, Amity University, Noida, Uttar Pradesh, India*

Abstract: Biosensors are an investigative contrivance used to find a chemical substance that combines an organic component with a physicochemical detector. Various biosensors are used in different fields: electrochemical-based, immune-based, magnetic-based, thermometric-based, acoustic-based, enzyme-based, optical-based, DNA-based, and tissue-based, *etc*. Enzyme-based biosensors are those which use enzymes or proteins for the recognition of elements and adjoining the inbuilt specificity of enzymes. Due to their high sensitivity and specificity, these enzymatic biosensors are frequently used in numerous fields, including the health and biomedical field. This book chapter will describe the various enzyme-based biosensors, their sensitivity and specificity, and their significant applications in different fields.

Keywords: Applications, Biosensors, Biomedical, Biotechnology, Enzymes, Quality indices.

INTRODUCTION

The arrangement of a biological element with a physiochemical element or appliance through a well-operational analytical device for the detection of a biological analysis is called a biosensor. A typical biosensor is principally comprised of an efficient transducer, a biological recognition element, and a signal processor, in which the biological recognition element can interact with the target molecule specifically, and then the transducer converts the biochemical information into a measurable signal [1].

Due to low instrumentation rate, high sensitivity, good accurateness, and ease to use, these biosensors are now gaining popularity in terms of commanding devices for sensing various analyses in different areas over conventional methods. As the physical, chemical, or biological reactions can be transformed into electrical,

* **Corresponding author Mridula Chaturvedi:** Amity Institute of Biotechnology, Amity University, Noida, Uttar Pradesh, India; E-mail: mridula.all@gmail.com

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

optical, or other signals by specific transducers, different kinds of biosensors are obtained according to the mode of signal transduction [2].

Similarly, the biosensors could also be classified based on the biological specificity conferring mechanism, the biocatalytic or affinity biosensors. In light of the monitoring analyses or reactions, the biosensors could be constituted by monitoring the concentration of analyses or reaction products directly or monitoring the inhibitor or activator of the bio-recognition element indirectly [3].

Thus on the discovery of these biosensors, a variety of bio-identified essentials like antibodies, nucleic acids, various fluids and different enzymes have been extensively used to make assorted biosensors. Historically, Clark and Lyons demonstrated the first biosensor *via* coupling the glucose. Determined by this revolutionary effort, the recognition of enzyme-based biosensors has full-grown extremely within the investigative population. As the key mechanism in the enzyme-based biosensors, enzymes possess outstanding bio-recognition potential and catalytic properties; that is, they could respond selectively to their matching substrates. Enzymes are not only the oldest but also the most common bio-recognition elements in current biosensors. In recent decades, enzyme-based biosensors have been proven to be a ground-breaking modus operandi in ailment finding, biological and biomedical study, and so forth [4].

Incorporated with dissimilar transducers, the enzyme-based biosensors could be primarily divided into electrochemical, optical, magnetic, tissue, DNA, RNA and other types. Given the speedy progress in this field, this chapter will introduce various enzyme-based biosensors and their important applications [5].

ENZYME-BASED BIOSENSORS

Enzymes are globular proteins largely composed of the 20 naturally occurring amino acids that can catalyze biochemical reactions and the recognized green catalysts with high specificity. The enzyme-based biosensor, as a precise type of biosensor, is also similarly made up of three parts; a bio-recognition element (enzyme), an effective transducer, and a digital signal processor. In other words, it depends on the collection of suitable enzymes as the bio-receptor molecules, skilled immobilization procedures, exact transducers, and lastly, integration of them in delicate forms to develop different kinds of biosensors. These well-established devices forever have high-quality immunity from meddling to complete the recognition of target biomolecules in a satisfactory range of concentrations [6].

The organization of an enzyme-based biosensor demands that the biocatalyst should be incorporated with the conductive electrodes so that the enzyme catalytic conversion in sequence can be transferred electronically. As a result, any electrical change at the conductive supporter, such as the depletion of reactants or the formation of products in the biocatalytic process, provides useful electronic transduction information of the biological reorganization event occurring at the electrode. On the other hand, the concentration of the target biomolecules is related to the decrement of the enzymatic product, as the enzymatic activity can be reserved by the detection objective [7]. It is of vital significance to immobilize the enzyme on the electrode during the manufacture of enzyme-based biosensors. The immobilization method must make sure the evenness of the active site, except to preserve the functionality and bioactivity of the biomolecules. Therefore, the immobilization technique can directly affect the sensitivity, selectivity, steadiness, and reproducibility of the constructed enzyme biosensor. With the requirement of a satisfactory enzyme biosensor, different kinds of immobilization techniques have been subjugated. These means can be classified into physical adsorption, covalent binding, entrapment within a polymerised matrix, and cross-linker [8]. Additionally, the biocatalytic activity of enzymes highly depends on the applied possible, temperature, and pH of the solution environment. All these factors can be credited to the concentration of substrate, the presence or absence of oxygen, and the properties of the enzyme. At the optimum pH and temperature, the greatest reproducibility and sensitivity are attained [9].

APPLICATIONS OF ENZYMATIC BIOSENSORS

Enzymatic biosensors can be used in different fields like the biomedical, food industry, biotechnology, microbiological, and healthcare field, *etc*., as described below:

Enzyme Biosensors for Biomedical Applications

Amperometric Enzyme Biosensors

Amperometric enzyme biosensors are commonly divided into three main classes, or generations, depending on the electron transfer method used for the measurement of the biochemical reaction or the degree of separation of the biosensor components (transducer, enzyme, mediators and cofactors). In all cases, the presence of an enzyme is required, and therefore, sensor performance relies on different parameters, such as working pH and temperature [10].

First-Generation Biosensors

First-generation biosensors measure the concentration of analyses and/or products of enzymatic reactions that diffuse to the transducer surface and generate an

CHAPTER 9

Recent Trends of Nanobiosensor in Agriculture

Dhitri Borah[1], Ravi Kumar Goswami[2], Avanish Kumar Shrivastav[3], Priti Giri[4], Neelesh Kumar[3] and **Tejveer Singh[5,*]**

[1] *Department of Zoology, Biswanath College, Biswanath Chariali, 784176, Assam, India*

[2] *Department of Zoology, Hindu College, University of Delhi, New Delhi- 110007 India*

[3] *Department of Biotechnology, Delhi Technological University, Delhi, 110042, India*

[4] *Department of Botany, University of Delhi, Delhi-110007, India*

[5] *Translational Oncology Laboratory, Department of Zoology, Hansraj College, University of Delhi, New Delhi, Delhi-110067, India*

Abstract: Sustainable agriculture has the potential to benefit greatly from nanobiosensors. Nanomaterials are crucial components of numerous biotic and abiotic remediation systems and have a huge impact on the mobility, fate and toxicity of soil contaminants in agriculture. It is believed that nanobiosensor have a revolutionary impact on the field of agriculture by focusing research and development toward the goals of achieving sustainable agriculture. Nanobiosensors have significant benefits such as improved recognition sensitivity or specificity, and retain immense promise for the application of nanobiosensor in various areas such as food quality and bioprocess control, agriculture, biodefense and medical applications. Nanobiosensors application in the agricultural area has significantly improved productivity. The economic and cutting-edge nanobiosensors have been emphasised in this book chapter to address the difficulties in the main agricultural industry and emphasize the significance of nanobiosensor to detect insecticides, herbicides, fertilizers and diseases for increasing crop yield.

Keywords: Agriculture, Biosensors, Nanotechnology, Nanoparticles, Nanobiosensors.

INTRODUCTION

Sustainable agriculture is important to accomplish the goal of sustainable development of the United Nations. Nanotechnology has demonstrated remarkable possibilities for promoting sustainable agriculture. The Food and Agriculture Organization (FAO, 2017) estimates the need for food by 50%,

* **Corresponding author Tejveer Singh:** Translational Oncology Laboratory, Department of Zoology, Hansraj College, University of Delhi, New Delhi, Delhi-110067, India; E-mail: Tej6875@gmail.com

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

particularly in emerging nations, to demolish the hunger of the world's population, which will reach 10 billion by 2050 [1].

Additionally, there are 815 million people who are malnourished presently and by 2050, it is predicted that the count will increase to 2 billion. The global agricultural systems need to be drastically changing in light of this circumstance. Recent studies have demonstrated the great future of nanotechnology to enhance the agricultural section by boosting the efficacy of farm production and providing solutions to challenges in agriculture and the environment to increase food yield and sustainability. Therefore, global food security has become crucial, and the application of nanotechnology has achieved importance in recent times. However, the process of increasing food production has the hazardous impact on agricultural ecosystems, including the persistence of residual pesticide particles, the excess of heavy metals, and pollutants with harmful elemental particles. A wide range of health implications, including disorders of the bone marrow and nervous system, metabolic issues, infertility, disruption of cellular biological processes, as well as respiratory and immunological conditions, due to ingestion of such toxic elements into living beings through agricultural products.

Nano-biosensors are tiny element devices created to distinguish between certain molecules, biological elements or environmental factors. These sensors can detect at a level far lower than their macro scale analogs, are portable, cost-effective, and have a high degree of specificity. The industries of agriculture and food are a prime source of earnings and services for a sizeable percentage of the people. The agricultural sector contributes significantly to self-sustaining economic growth by giving humans the consumables they need and the raw materials for industrialization. The objective of a sensor is to identify changes in the environment, such as changes in temperature, humidity, water flow or light intensity, and to transmit the information to another electrical instrument that can analyze it. Nanobiosensors are characterized by their compactness, minimal rates, bio-compatibility, non-toxicity, portability, specificity, resilience, quick reaction times, absence of electrical noise, accuracy, precision, and reproducibility at optimal temperature and pH [2]. Nanobiosensors are used in agriculture to detect toxicants, pesticides, pollutants, veterinary medicines and heavy metals in food as well as direct and indirect food-borne pathogenic bacteria. Additionally, nanobiosensors can also identify antibiotic resistance, soil quality, crop stress and food quality [3]. In agriculture, nanobiosensors can be utilized to detect metal ions, a wide range of diseases, phytohormones, crop metabolites, insecticides, herbicides, pH and moisture of the soil. Nanobiosensors could enhance sustainable and healthy agriculture when it is used effectively with proper regulation and management. This chapter aims to provide a brief overview of the advancement and application of nanobiosensor in the field of agriculture.

BIOSENSOR

Biosensor is a tool that can identify various substances in biological or dietary samples, including environmental contaminants, vitamins, pesticide waste and biomolecules [4 - 9]. Biosensor is a tool of three components, including a bio-element, a transducer and a reading system (Fig. **1**). A bio-receptor is a biological living system like an organism, tissue and cell, or several biological components, including DNA/RNA, enzymes, receptors, peptide nucleic acids (PNA), antibodies and locked nucleic acids (LNA), organs, organelles, microbes, *etc*. make use of a biological mechanism for the recognition of analyte. The special interactions between the analyte and the receptor, such as enzymes-substrate (enzymatic interaction), microorganisms-proteins (cellular interaction), two complementary strands of nucleic acid (nucleic acid interactions) and antigen-antibody interaction [10 - 15], are converted into measurable effect by the transducers. Finally, such interactions are measured by a proper reading system (biosensor monitors) as shown in Fig. (**1**). These small devices are also classified according to how the signal transduction mechanism is used into many categories, including optical, electrochemical, piezoelectric, pyroelectric, electronic and gravimetric biosensors Many researchers are working to incorporate nanoparticles into biosensors construction to enhance the precision and functioning of a biosensor. Improvement in biosensor materials can play a significant role in the better application of sensing technology.

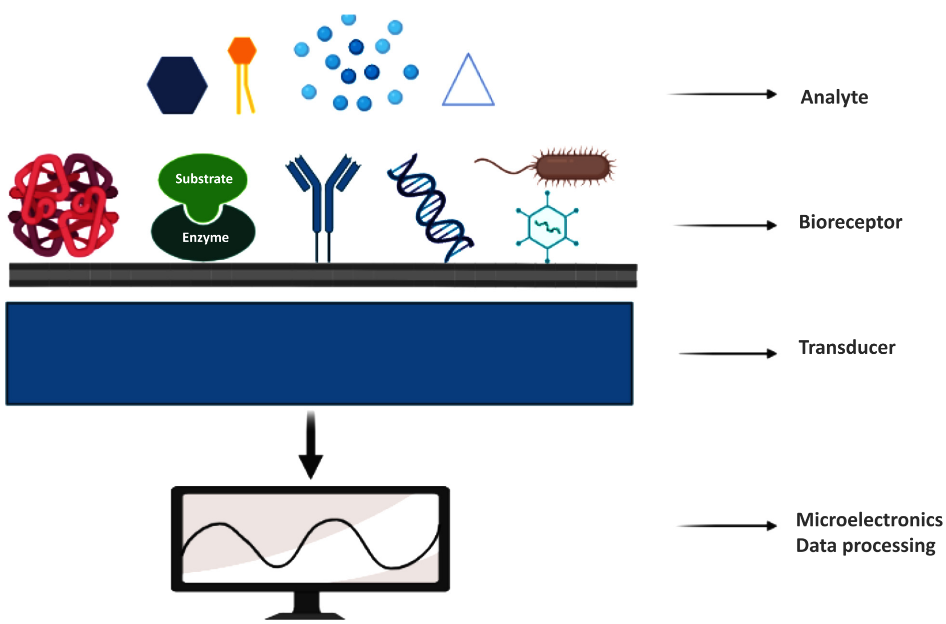


Fig. (1). Schematic diagram of the components of Biosensor.

SUBJECT INDEX

A

B

Vivek K. Chaturvedi, Dawesh P. Yadav and Mohan P. Singh (Eds.)

C

D

E

F

G

H

I

R

S

T

V

W

Y

Vivek K. Chaturvedi

Dr. Vivek K. Chaturvedi is a young-scientist fellow in the Department of Health Research, Ministry of Health and Family Welfare at the Institute of Medical Sciences, Banaras Hindu University, Varanasi- India. He earned Ph.D. in biotechnology from the University of Allahabad Prayagraj, India. He became a postdoctoral researcher in the Department of Gastroenterology, IMS-BHU, Varanasi. Dr. Chaturvedi is actively engaged in drug delivery, tissue engineering, synthesis and functionalization of bio-nanomaterials as well as their fabrication for the development of various biosensors. He has voluntarily served as a reviewer, published many original articles in peer-reviewed high-impact journals along with many international books, magazine articles, and chapters.

Dawesh P. Yadav

Prof. Dawesh P. Yadav is presently working as associate professor of gastroenterology at Banaras Hindu University, Varanasi (India). He did M.B.B.S. and M.D. (Gen. Medicine) from Institute of Medical Sciences (IMS), B.H.U. Varanasi, India. He is a member of Indian National Association for Study of Liver (INASL), Indian Society of Gastroenterology and received many other prestigious awards. Prof. Yadav worked as a senior resident in All India Institute of Medical Sciences (AIIMS), New Delhi from 2013-2017. He joined as assistant professor in I.M.S., B.H.U. in 2017. In 2019, he was promoted as associate professor in the department of gastroenterology; I.M.S.-B.H.U. He has conducted research on various aspects of inflammatory bowel disease, liver cirrhosis and nanobiotechnology over a decade. He has published a number of research papers and book chapters in peer-reviewed high impact journals. He has currently edited editorial books of Bentham Science Publishers. He has been serving as an editorial board member in many reputed journals.

Mohan P. Singh

Prof. Mohan P. Singh is presently working as a professor and coordinator in the Centre of Biotechnology at the University of Allahabad, Prayagraj (India). He completed Ph.D. from Panjab University Chandigarh, India. He joined as a lecturer in HNB Garhwal University in Botany in 1992. In 2000, he moved to the Department of Biotechnology at VBS Purvanchal University, Jaunpur where he became a reader in 2000 and professor in 2008. In 2013, Prof. Singh joined the University of Allahabad, Prayagraj. His research area is microbial and mushroom biotechnology. He is a visiting professor in the Department of Chemistry & Biochemistry at the University of Maryland Baltimore County UMBC), USA. He has over 30 years of teaching experience and 35 years of research experience. He has published a number of papers and book chapters and edited books. Prof. Singh has completed 7-research projects and presently has one project in hand. He is a fellow of AEB and BRITS. He has been conferred with the Award of Excellence by Allahabad University along with many other accolades. Besides, due to the impressive academic career Prof. Singh has a wide range of administrative experience as head, coordinator, chief proctor, professor in-charge library, member of the academic council in various universities. He has also been on the editorial board of many prestigious journals.