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Laboratory Applications of Electrochemical Biosensors in Detecting Parkinson's Disease Early

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Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting millions worldwide. Early diagnosis is crucial for effective disease management, but current diagnostic methods face challenges such as low sensitivity, high costs, and the need for specialized equipment. Electrochemical biosensors have emerged as promising tools for early PD detection by identifying specific biomarkers associated with the disease. These devices convert biological reactions into measurable electrical signals, enabling sensitive and selective analyte detection. Recent advancements in nanomaterials and sensing mechanisms have significantly enhanced the performance of electrochemical biosensors for PD biomarker detection. Key biomarkers include alpha-synuclein (α-syn), a primary component of Lewy bodies; microRNAs such as miR-195; dopamine, a critical neurotransmitter; and PARK7/DJ-1 protein. Innovative biosensor designs, such as aptamer-based liquid crystal biosensors for α-syn detection and nanomaterial-modified electrodes for miR-195 quantification, have demonstrated high sensitivity and selectivity. Additionally, flexible electrodes and microfluidic sensors have been developed for dopamine monitoring, while impedance spectroscopy has been employed for PARK7/DJ-1 detection. The integration of electrochemical biosensors with digital health platforms and machine learning tools holds promise for personalized medicine in PD management. However, standardization

and validation of these technologies are necessary for widespread clinical adoption. With ongoing advancements, electrochemical biosensors have the potential to revolutionize early diagnosis and monitoring of PD, ultimately improving patient outcomes and quality of life.
Keywords: laboratory testing, PD, Parkinson disease

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder that primarily affects the motor system, leading to symptoms such as tremors, rigidity, bradykinesia, and postural instability. With a global prevalence estimated at over six million individuals, PD represents a significant health issue, particularly among the elderly population (Mobed et al., 2021). The pathophysiology of PD is characterized by the degeneration of dopaminergic neurons within the substantia nigra, a brain region integral to movement control. While the precise etiology of the disease remains unclear, it is believed to arise from a complex interplay of genetic and environmental factors. Early detection of PD is crucial for effective disease management and therapeutic intervention. However, current diagnostic methodologies, which rely on the clinical evaluation of symptoms and standard laboratory tests, face several challenges, including low sensitivity, high costs, and the need for specialized equipment. As a result, there is an increasing demand for innovative diagnostic tools capable of accurately detecting PD in its early stages. Electrochemical biosensors have emerged as promising candidates for the early diagnosis of PD. These devices convert biological reactions into measurable electrical signals, facilitating both qualitative and quantitative assessments of PD biomarkers (Hosseini et al., 2022). Advances in nanotechnology and material science have led to the development of novel sensing platforms that offer enhanced sensitivity and selectivity. Alpha-synuclein (α-syn), a key biomarker for PD, forms aggregates in the brains of affected individuals and is considered a hallmark of the disease. Numerous studies have focused on the development of electrochemical biosensors for detecting α-syn in biological samples. For example, a recent study introduced a gold nanoparticle-modified graphene immunosensor for the ultrasensitive and specific detection of α-syn in human plasma, achieving a lower limit of quantification of 4 ng/mL. Dopamine (DA), a neurotransmitter that is depleted in PD patients due to the loss of nigrostriatal neurons, is another important biomarker for the disease (Kujawska et al., 2021). Monitoring DA levels can aid in early PD diagnosis and in optimizing dopamine replacement therapy. Graphene-based biosensors, known for their high conductivity and large surface area, have shown significant promise in detecting DA. A novel approach involving the periodic stacking of positively charged NiAl layered double hydroxide (LDH) nanosheets with negatively charged graphene monolayers has resulted in a biosensor exhibiting exceptional electrocatalytic properties for DA detection. MicroRNAs (miRNAs), small non-coding RNAs that play a role in gene regulation, have also been identified as potential biomarkers for PD. A developed electrochemical nanobiosensor, based on exfoliated graphene oxide (EGO) and gold nanowires (GNWs), enables early PD detection by quantifying circulating miR-195, a miRNA associated with PD. This nanobiosensor demonstrated high sensitivity, with a detection limit of 2.9 femtomolar. Aptasensors, which use aptamers (short single-stranded DNA or RNA molecules that bind to specific targets), offer several advantages, including portability, ease of use, and the ability for real-time analysis, making them suitable for point-of-care diagnostics (Mikuła et al., 2022). Recent studies have explored innovative aptasensors for the detection of PD biomarkers and discussed potential analytical platforms for preclinical diagnosis. In addition to α-syn and DA, other PD biomarkers, including urate, ascorbic acid, and various miRNAs, have been investigated for their diagnostic potential. A comprehensive review has compared the properties of electrochemical, optical, and optochemical biosensors for detecting these biomarkers. Nanomaterials such as gold

nanoparticles (AuNPs), quantum dots (QDs), and carbon nanotubes (CNTs) have greatly advanced the development of electrochemical biosensors for PD diagnosis. These materials enhance the electrochemical activity of the sensing platform, improving sensitivity and lowering detection limits. For instance, a study developed an immuno-platform using gold nanoparticles conjugated with graphene for the sensitive detection of α-syn, demonstrating synergistic effects that enhanced electrochemical activity. Electrochemical biosensors hold significant promise for the early diagnosis of Parkinson's Disease. The continuous progress in nanotechnology and material science has led to the creation of novel sensing platforms that offer enhanced sensitivity and selectivity (Ganesh et al., 2016). The detection of key PD biomarkers using electrochemical biosensors provides a reliable, rapid, and cost-effective approach for the early diagnosis and monitoring of the disease. Ongoing research and development in this field are critical for the commercialization of these biosensors and their integration into clinical practice, ultimately improving the management and treatment of Parkinson's Disease. This review examines various biomarkers for Parkinson's disease and underscores the transformative potential of electrochemical biosensors in early detection. These advancements may lead to innovative diagnostic platforms and personalized healthcare solutions.

Diagnosis of Parkinson's Disease

Parkinson's disease (PD) is a chronic neurodegenerative disorder characterized by a variety of motor and non-motor symptoms. The diagnosis of PD is primarily clinical, based on the identification of key motor symptoms (Postuma et al., 2015). Both genetic and environmental factors play a role in the pathogenesis of PD, although the exact cause remains unknown. Inherited genetic variants are responsible for approximately 5% of cases, with mutations in the GBA gene commonly associated with familial PD. Environmental factors also contribute to disease risk, as epidemiological evidence links occupational exposure to pesticides and heavy metals with an increased incidence of PD (Smith, 2022). Oxidative stress caused by free radicals generated during normal cellular metabolism may contribute to neurodegeneration in dopamine-producing neurons in the substantia nigra. Advanced age is the strongest risk factor, with incidence rates rising steadily after the age of 50. While the causal mechanisms have not yet been fully defined, a combination of genetic predisposition, aging, and environmental toxins is thought to trigger progressive loss of nigral cells via oxidative stress and mitochondrial dysfunction (Toomey, 2022) (Prasuhn, 2021). Clinically, the diagnosis of PD depends primarily on the recognition of characteristic motor symptoms. Bradykinesia, which manifests as slowed initiation and execution of movement along with difficulties in fine motor control, often appears early in the disease. Rigidity, presenting as either "cogwheeling" or "lead pipe" resistance to passive limb movement, develops concurrently. Resting tremor, frequently the initial symptom, involves a unilateral 4-6 Hz "pill-rolling" motion of the hand or fingers at rest. The presence of at least two of these cardinal symptoms, in the absence of an alternative diagnosis, constitutes the diagnostic criteria for idiopathic Parkinson's disease. While these clinical signs are essential, diagnosing PD remains challenging, especially in the early stages of the disease, and misdiagnosis remains relatively common. This underscores the need for supplementary diagnostic tools to enhance diagnostic accuracy and enable earlier intervention (Rizzo et al., 2016).

Clinical criteria and diagnostic accuracy

Ongoing research aims to further refine the MDS diagnostic criteria for Parkinson's Disease (PD). Promising developments in this area include the integration of quantitative measurements of motor signs through digital tools such as wearable sensors. By objectively tracking parameters such as fine motor skills, gait, and tremor over time, these tools have the potential to identify subtle deficits earlier than traditional clinical examinations. Additionally, neuroimaging and fluid biomarkers are showing promise in complementing physical signs.

Dopaminergic neuroimaging, such as DAT SPECT/PET scans, allows for the objective measurement of lost nigrostriatal neurons in PD patients, which can be differentiated from controls (Postuma et al., 2015). Current research is also focused on candidate fluid biomarkers, including various forms of alpha-synuclein, DNA methylation profiles, metabolite levels, and protein aggregates, which can be detected in blood, cerebrospinal fluid (CSF), or other biosamples. Advances in genetic research may lead to more personalized diagnostic approaches. As additional causative genes for Mendelian or sporadic forms of parkinsonism are identified, genetic testing panels could allow for the identification of individuals at risk of developing PD before classic motor symptoms emerge. Furthermore, polygenic risk scores that combine multiple risk variants show promise in predicting the development of PD even in asymptomatic individuals. The integration of multiple diagnostic tools may optimize sensitivity and specificity, surpassing the efficacy of individual modalities. Machine learning approaches that combine clinical, imaging, fluid, genetic, and sensory data could reveal subtle disease-associated patterns that are not apparent to experts. The “Digital Biomarker” paradigm holds significant potential for earlier and more accurate diagnosis of PD and atypical parkinsonism, even before neurodegeneration occurs. Continued international collaboration, such as through consortia like the MDS, will help refine diagnostic criteria in light of these evolving diagnostic modalities. The ultimate goal is to facilitate the development of disease-modifying therapies, making early and accurate diagnosis a key research priority for optimizing patient outcomes and evaluating novel treatments.

Non-motor symptoms and early diagnosis

Non-motor symptoms, including autonomic dysfunction, cognitive impairments, sleep disturbances, and sensory anomalies, are increasingly recognized as critical components in the diagnosis of PD (Tolosa et al., 2021). These symptoms often precede motor manifestations and can provide early indicators of the disease. The concept of prodromal PD, which encompasses these early non-motor symptoms, has been integrated into the MDS diagnostic criteria to promote earlier identification of the disease (Marsili et al., 2018). However, the subtle and variable nature of these symptoms presents challenges in early diagnosis, and they are frequently overlooked in clinical practice (Mei et al., 2021).

Role of biomarkers and imaging

The search for reliable biomarkers and imaging techniques to improve the accuracy of PD diagnosis continues to progress. Genetic testing, olfactory testing, MRI, and dopamine-transporter single-photon-emission computed tomography (SPECT) imaging are among the adjunctive tests showing promise in assisting clinical diagnostic decisions. These tools are particularly useful in distinguishing PD from other parkinsonian syndromes and identifying individuals at higher risk of developing the disease. Despite these advancements, no definitive biomarker for PD has been established, and the diagnosis remains predominantly clinical (Kobylecki, 2020).

Machine learning and diagnostic innovations

Recent advancements in machine learning provide new opportunities for improving PD diagnosis. Machine learning algorithms can analyze complex datasets, including both motor and non-motor symptoms, genetic information, and imaging data, to differentiate PD from other conditions with similar clinical presentations. These methods have shown significant potential for enhancing diagnostic accuracy and are being increasingly incorporated into clinical practice. However, their widespread adoption will require further validation and standardization. The diagnosis of Parkinson's Disease is a complex and evolving field. While clinical criteria remain the foundation of diagnosis, the integration of non-motor symptoms,

biomarkers, and advanced imaging techniques is enhancing diagnostic accuracy. Machine learning offers promising new tools for early and accurate diagnosis, but further research and validation are necessary. As our understanding of PD continues to grow, ongoing revisions of diagnostic criteria and the development of novel diagnostic tools will be crucial for improving early detection and patient outcomes.

Biomarkers for Parkinson's disease detection

Accurate and early diagnosis of PD is critical for effective treatment and management. However, current diagnostic methods, which primarily rely on clinical history and physical examination, frequently lead to misdiagnosis, particularly in the early stages of the disease. The identification of reliable biomarkers for PD has the potential to revolutionize early diagnosis, improve monitoring of disease progression, and enhance the effectiveness of therapeutic interventions (Rees et al., 2018). This section examines the emerging significance of various biomarkers in detecting Parkinson's disease, with a focus on CSF and blood-based biomarkers, extracellular vesicles (EVs), and neuroimaging techniques.

Cerebrospinal fluid biomarkers

Cerebrospinal fluid (CSF) biomarkers hold substantial promise for the early detection, diagnosis, and monitoring of Parkinson's Disease (PD). Due to the inaccessibility of brain tissue for direct analysis, CSF, which circulates around the brain and spinal cord, provides an invaluable window into the biochemical changes occurring in the central nervous system throughout the course of the disease. Numerous studies have identified various proteins, metabolites, and other molecules within the CSF that are associated with the pathophysiology of PD, presenting potential as both diagnostic and prognostic biomarkers. One of the most extensively researched CSF biomarkers in PD is alpha-synuclein, a protein that misfolds and aggregates in the brains of PD patients. Alpha-synuclein appears in multiple forms within the CSF, including total alpha-synuclein, oligomeric alpha-synuclein, and phosphorylated alpha-synuclein, with oligomeric alpha-synuclein showing particular promise in distinguishing PD patients from healthy controls. Elevated levels of oligomeric alpha-synuclein have been associated with disease progression, and some studies suggest its potential as a predictive biomarker for PD even in the prodromal stages. In addition to alpha-synuclein, neurofilament light chain (NfL) has emerged as an important marker for differentiating PD from other neurodegenerative conditions, particularly atypical parkinsonian syndromes such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP). CSF levels of NfL are typically elevated in these conditions compared to PD, making it a valuable biomarker for differential diagnosis. Moreover, higher NfL levels have been correlated with more rapid disease progression and cognitive decline in PD patients. Metabolomic studies have also revealed alterations in CSF metabolites among PD patients. Disruptions in purine metabolism and tryptophan metabolism have been observed, suggesting that metabolic pathways play a role in the pathogenesis of PD. These findings are especially noteworthy, as they suggest systemic changes in PD that extend beyond the well-documented alpha-synuclein pathology. For example, decreased levels of the purine metabolite urate—an antioxidant—have been linked to faster disease progression and a greater risk of developing PD. The neuroprotective properties of urate have generated interest in its potential as both a biomarker and a therapeutic target. Markers of oxidative stress have also attracted attention, given the established role of oxidative damage in PD pathology. Elevated levels of oxidative stress markers, such as 8-hydroxy-2′-deoxyguanosine (8-OHdG) and F2-isoprostanes, have been identified in the CSF of PD patients and are linked to disease severity. These markers offer valuable insight into the neurodegenerative processes and could serve as indicators of disease progression. Furthermore, PD is not only a movement disorder but also involves significant cognitive decline, particularly in the later stages. Amyloid-beta (Aβ) and tau proteins, which are well-established biomarkers for Alzheimer's disease, have also been implicated in cognitive decline in PD patients. Elevated

CSF levels of phosphorylated tau (p-tau) and total tau (t-tau) have been associated with worsening cognitive function and an increased risk of developing Parkinson's Disease Dementia (PDD). Similarly, lower levels of CSF Aβ42, a marker of amyloid pathology, have been linked to cognitive impairment in PD, suggesting that overlapping neurodegenerative processes contribute to dementia in PD (Chen, 2020) (Schirinzi, 2022). Given the heterogeneity of PD, it is likely that no single biomarker will be sufficient for accurate diagnosis or prognosis. Instead, a combination of biomarkers—such as alpha-synuclein, NfL, oxidative stress markers, and amyloid/tau proteins—may provide a more comprehensive diagnostic and prognostic model. Panels of CSF biomarkers that assess various aspects of PD pathology, including synuclein aggregation, neurodegeneration, inflammation, and oxidative stress, have demonstrated improved diagnostic accuracy in early-stage PD. However, while these findings are promising, further validation in larger, independent cohorts is necessary to confirm their clinical utility and ensure that these biomarkers can be reliably applied in routine practice. CSF biomarkers offer a valuable tool for advancing the understanding of PD and improving diagnostic accuracy, particularly in the early stages when clinical symptoms may be subtle or non-specific. The identification of specific proteins and metabolites in CSF, such as oligomeric alpha-synuclein, NfL, and oxidative stress markers, has the potential to revolutionize the diagnosis and monitoring of PD. However, the field remains in development, and further research is required to validate these biomarkers in diverse patient populations and establish standardized protocols for their clinical use (Andersen et al., 2017).

Blood-Based biomarkers

Blood-based biomarkers offer a non-invasive alternative for the early diagnosis and monitoring of PD. A wide array of studies have explored the potential of various proteins and molecular markers in blood samples. For example, blood alpha-synuclein species and neurofilament light chain are being investigated for their ability to provide early and differential diagnoses of PD, particularly in comparison to atypical parkinsonian disorders (Parnetti et al., 2019). Additionally, research has identified several downregulated mRNAs (SDHC, CDC42, NDUFS1, COX4I1, and MAPK8) and miRNAs (miR-29a-3p, miR-19-3p, and miR-126-5p) as potential diagnostic markers for PD. Furthermore, plasma-based circulating microRNAs (miRNAs) have shown promise as biomarkers for PD. A study identified a panel of PD-predictive biomarkers, including miR-1826/miR-450b-3p, miR-626, and miR-505, which demonstrated high predictive power in a replication set. However, the predictive values were lower in the validation set, highlighting the challenges associated with molecular biomarker research using samples from multiple clinical sites (He et al., 2018).

Extracellular vesicles

Extracellular vesicles (EVs) have garnered attention as a potential source for developing biomarkers in Parkinson’s disease. These vesicles are capable of transporting proteins and molecular substances from the central nervous system to peripheral regions, making them detectable in easily accessible biological samples such as blood, urine, and saliva. A comprehensive review and meta-analysis have identified various proteins and ribonucleic acids within EVs from Parkinson’s disease patients, with alpha-synuclein (aSyn) and leucine-rich repeat kinase 2 (LRRK2) being the most extensively studied. The analysis revealed a significant increase in EV aSyn levels in neuronal L1 cell adhesion molecule (L1CAM)-positive blood EVs from Parkinson’s disease patients when compared to healthy individuals (Xylaki et al., 2023). This finding suggests that CNS-derived EVs present in blood could be pivotal in the future development of biomarkers for Parkinson’s disease.

Neuroimaging biomarkers

Neuroimaging techniques have demonstrated considerable potential as biomarkers for Parkinson's disease (PD). Various imaging modalities, such as magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT), have been investigated for their ability to monitor disease progression and enhance clinical care. The identification and validation of reliable biomarkers for Parkinson's disease are critical for facilitating early diagnosis, tracking disease progression, and evaluating the effectiveness of therapeutic interventions. Both cerebrospinal fluid (CSF) and blood-based biomarkers, extracellular vesicles, and neuroimaging techniques have all shown promise in this regard (Surguchov, 2022). However, further research and validation in large, independent cohorts are required to substantiate their clinical utility. Combining multiple biomarkers from different modalities may represent the most effective approach to enhancing diagnostic accuracy and promoting personalized medicine in the management of Parkinson's disease. Early diagnosis of PD remains a substantial challenge in the medical field. Conventional diagnostic methods, which typically rely on the evaluation of clinical manifestations and movement disorders by neurologists, have several limitations, including low sensitivity and specificity, high costs, and the necessity for advanced equipment. This has stimulated growing interest in the development of novel diagnostic tools capable of detecting PD in its early stages. One promising solution to these challenges is the use of electrochemical biosensors. These biosensors have demonstrated great potential in the early detection of PD by identifying specific biomarkers associated with the disease. For example, a highly sensitive electrochemical nanobiosensor has been developed to detect miR-195, a circulating biomarker for PD. This biosensor utilizes exfoliated graphene oxide and gold nanowires to modify the surface of a screen-printed carbon electrode, achieving an impressive detection limit as low as 2.9 femtomolar. Similarly, another innovative biosensor integrates the stimuli-responsiveness of liquid crystals with the specific interaction of a DNA aptamer to detect alpha-synuclein, a protein linked to PD. This biosensor demonstrates high sensitivity, with a detection limit of 10 pM, marking it as a promising tool for early diagnosis. Furthermore, electrochemical aptasensors have been highlighted for their portability, ease of use, and ability to perform real-time analysis. These aptasensors are designed to detect a variety of PD biomarkers, including alpha-synuclein, dopamine, and urate, among others. Advancements in nanomaterials have significantly improved the performance of these biosensors, enabling the detection of multiple biomarkers in clinically relevant samples in real-time. While early diagnosis of Parkinson's disease remains challenging, the development of electrochemical biosensors offers a promising solution. These biosensors provide sensitive, rapid, reliable, and cost-effective diagnostic tools that could potentially revolutionize the early detection and monitoring of PD.

Electrochemical biosensors

Electrochemical biosensors have emerged as a powerful tool in medical diagnostics, offering several advantages over traditional diagnostic methods. These sensors capitalize on the principles of electrochemistry to detect and quantify specific biomolecules, providing a rapid, sensitive, and cost-effective approach to disease diagnosis and monitoring (Vatankhahan et al., 2024).

One of the key advantages of electrochemical biosensors is their ability to detect biomarkers at extremely low concentrations. Many disease-associated biomarkers, such as proteins, hormones, and nucleic acids, exist in very small quantities in biological samples, making them challenging to detect using conventional techniques. However, electrochemical biosensors can amplify the signal generated by these low-concentration analytes, enabling the early detection of diseases even before clinical symptoms manifest. This is particularly crucial for conditions such as cancer, neurodegenerative disorders, and infectious diseases, where early intervention can significantly enhance patient outcomes.

The working principle of electrochemical biosensors is based on the interaction between a biological recognition element (e.g., enzymes, antibodies, nucleic acids) and the target analyte. Upon binding of the analyte to the recognition element, an electrochemical reaction is triggered, generating a measurable signal, such as a change in current, voltage, or impedance. This signal is then amplified and processed by the sensor's electronic circuitry, providing a quantitative readout of the analyte's concentration.

A notable advantage of electrochemical biosensors is their versatility. These sensors can be designed to detect a wide array of biomolecules, including glucose, hormones, proteins, nucleic acids, and even entire cells or pathogens. This flexibility facilitates the development of diagnostic tools capable of simultaneously monitoring multiple biomarkers, offering a more comprehensive assessment of a patient's health status (Wang et al., 2020). Additionally, electrochemical biosensors can be miniaturized and incorporated into portable, handheld devices, making them ideal for point-of-care (POC) testing. This is particularly advantageous in situations where rapid diagnosis is critical, such as emergency settings or regions with limited resources. These POC devices can deliver immediate results, enabling healthcare professionals to make timely decisions and initiate appropriate treatments.

Another key advantage of electrochemical biosensors is their cost-effectiveness. In comparison to traditional laboratory-based diagnostic methods, which often require expensive equipment and specialized personnel, electrochemical biosensors can be produced at a relatively low cost. This makes them more accessible to a broader range of healthcare providers and patients, particularly in developing regions where access to advanced medical technologies may be limited.

Beyond their diagnostic applications, electrochemical biosensors are also being utilized for therapeutic monitoring. By continuously tracking the levels of specific biomolecules, these sensors can assist healthcare providers in adjusting medication dosages, evaluating the effectiveness of treatments, and detecting potential adverse effects in real time. The performance of electrochemical biosensors has been further enhanced by the integration of nanomaterials, such as carbon nanotubes, graphene, and metal nanoparticles. These nanomaterials can improve the sensitivity, selectivity, and stability of the sensors, in addition to facilitating the immobilization of the biological recognition elements. For instance, the incorporation of gold nanoparticles into electrochemical immunosensors has been demonstrated to enhance the detection of various disease biomarkers, including cancer-related proteins and viral antigens.

The convergence of electrochemical biosensors with wearable technologies has opened new avenues for continuous, non-invasive monitoring of physiological parameters. Wearable devices capable of detecting biomarker levels in biofluids such as sweat, tears, or interstitial fluid provide real-time insights into an individual's health status. This data can be leveraged for early disease detection, chronic condition management, and personalized treatment strategies (Sharma et al., 2021).

Despite the numerous advantages of electrochemical biosensors, there are still challenges that need to be addressed. One primary concern is the potential for interference from other substances in the biological sample, which could affect the specificity and accuracy of the sensor. Researchers are investigating various strategies, such as utilizing selective recognition elements and advanced signal processing algorithms, to mitigate this issue. Another challenge involves the need for reliable and reproducible sensor fabrication processes. Ensuring consistent performance across different biosensors is essential for their widespread adoption in clinical practice. Advances in microfabrication techniques and the development of standardized manufacturing protocols are helping to address this concern (Singh et al., 2021).

Looking ahead, the continued advancement of electrochemical biosensors is expected to have a transformative impact on the field of medical diagnostics. As research progresses, it is anticipated that more sensitive, selective, and user-friendly devices will emerge, capable of providing rapid, accurate, and cost-effective diagnosis and monitoring across a broad spectrum of diseases. These developments have the potential to revolutionize healthcare by enabling earlier intervention, personalized treatment, and improved patient outcomes. Electrochemical biosensors offer considerable benefits in the medical diagnostics field, including their ability to detect low-concentration biomarkers, versatility in analyte detection, and potential for miniaturization and integration into portable devices. These attributes make them valuable tools for early disease detection, therapeutic monitoring, and personalized healthcare. As the technology evolves, the impact of electrochemical biosensors on the future of healthcare is expected to be profound.

Electrochemical Biosensors for Parkinson's Disease Detection

Parkinson's disease (PD) is a neurodegenerative condition characterized by the degeneration of dopaminergic neurons, making early diagnosis critical for effective disease management. Electrochemical biosensors have garnered significant interest as potential diagnostic tools for PD due to their ability to detect specific biomarkers associated with the disease. These devices operate by converting biological recognition events into measurable electrical signals, enabling highly sensitive and selective detection of analytes. Recent studies have demonstrated the potential of electrochemical biosensors in identifying PD biomarkers, underscoring their applicability in early diagnosis and personalized treatment strategies (Chauhan et al., 2021).

Detection of Alpha-Synuclein

Alpha-synuclein (α-syn) is a major biomarker for PD, as it is a primary component of Lewy bodies found in the brains of individuals with the disease. Several studies have focused on developing electrochemical biosensors for detecting α-syn. For instance, a review highlighted the use of aptamers and antibodies in combination with various nanomaterials to create biosensors capable of detecting α-syn and studying its interactions with biometals and small molecules. Another study developed a liquid crystal biosensor that combines the specific interaction between a DNA aptamer and α-syn, achieving a detection limit as low as 10 pM. Additionally, a thin-film transistor (TFT) biosensor based on indium gallium zinc oxide (IGZO) has been proposed for early detection of α-syn, demonstrating high sensitivity and selectivity.

Detection of miR-195

MicroRNAs (miRNAs) have been widely explored as potential biomarkers for PD, with miR-195 receiving particular attention. A highly sensitive electrochemical nanobiosensor was developed to quantify circulating miR-195 for early disease detection. This biosensor, which utilized a screen-printed carbon electrode modified with exfoliated graphene oxide (EGO) and gold nanowires (GNWs), demonstrated an exceptional detection limit of 2.9 femtomolar. The biosensor's selectivity for target miRNA and its robustness in complex biological matrices, such as human serum, position it as a promising candidate for clinical diagnostics.

Detection of Dopamine

Dopamine (DA) plays a critical role as a neurotransmitter in PD, making its detection essential for monitoring disease progression and evaluating treatment effectiveness. Researchers have developed flexible platinum electrodes on bio-based poly(ethylene terephthalate) (Bio-PET) substrates for DA detection. These electrodes demonstrated a linear detection range from 3.5×10^{-5} mol/L to 8.0×10^{-4} mol/L, with a detection limit of 5.1×10^{-6} mol/L. Furthermore, a microfluidic electrochemical sensor has been reported for detecting DA in cerebrospinal fluid (CSF) and blood in a PD mouse model. This sensor functioned within a

range of 0.1–1000 nM DA, required only approximately 2.4 µL of sample volume, and successfully monitored changes in DA levels following L-DOPA treatment (Senel et al., 2020).

Detection of PARK7/DJ-1

PARK7/DJ-1 is another important biomarker for PD. Electrochemical impedance spectroscopy has been employed to detect PARK7/DJ-1 after electrode functionalization with specific antibodies. The developed sensor exhibited a linear response from 40 ng/mL to 150 ng/mL with a detection limit of 7.5 ng/mL. This method offers an alternative approach to diagnosing PD by measuring PARK7/DJ-1 concentrations in the human body.

Detection of Chloride Ions

Chloride ions have been implicated in the pathophysiology of PD. To enable in vivo monitoring of chloride levels, a novel electrochemical microbiosensor (ECMB) was developed using silver nanoparticles self-assembled onto Ti_3C_2Tx. This sensor demonstrated superior selectivity, accuracy, and reproducibility for chloride detection. The findings suggest that this ECMB, fabricated through a simple and reproducible method, could serve as a valuable tool for real-time monitoring of chloride concentrations in the PD mouse brain (Li et al., 2021).

Conclusion

Electrochemical biosensors represent a transformative advancement in the early diagnosis and monitoring of Parkinson's Disease (PD). By offering sensitive, specific, and cost-effective tools for the detection of PD biomarkers such as alpha-synuclein, dopamine, and miRNAs, these technologies address key limitations of conventional diagnostic approaches. The integration of advanced nanomaterials and innovative sensing mechanisms has further enhanced the performance and applicability of these biosensors, paving the way for their clinical adoption.

As research continues, the convergence of electrochemical biosensors with digital health platforms and machine learning tools holds the potential to revolutionize personalized medicine for PD. These developments will enable more accurate diagnoses, timely interventions, and improved therapeutic outcomes. Moving forward, the standardization and validation of biosensor technologies will be critical to their widespread clinical implementation, ultimately improving the quality of life for individuals affected by PD.

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