Iranian Journal of Analytical Chemistry
Volume 12, Issue 2, September 2024 (29--51) Original Research Article

مجله ایرانی شیمی تجزیه
دوره ۱۲، شماره ۲، مهر ماه ۱۴۰۴ (۵۱-۲۹)

Electrochemical Biosensing of miRNAs for Early Breast Cancer Detection: A Comprehensive Review

Elham Sahebnazar[1], Solmaz Kia[2]*, Sina Jafari Dargahlou[1]

1. Department of Biophysics, Faculty of Advanced Technologies, University of Mohaghegh Ardabili, Ardabili, Namin, Iran.
2. Department of Engineering Sciences, Faculty of Advanced Technologies, University of Mohaghegh Ardabili, Namin, Iran.

Received: 13 August 20205 Accepted: 18 September 2025

DOI: 10.30473/ijac.2026.77335.1342

Abstract

Breast cancer, a significant global health concern, has seen 2.3 million new cases and 700,000 deaths in 2020. Traditional diagnostic methods, such as mammography, ultrasound, and MRI, have limitations, necessitating the development of innovative, non-invasive tools. This article explores the potential of miRNA-based electrochemical biosensors for early detection of breast cancer, focusing on their reliability, sensitivity, selectivity, affordability, and personalized medicine. Using databases like PUBMED, Science Direct, ACS, Springerlink, Taylor & Francis, and Google Scholar, a thorough literature search was carried out in December 2025. Electrochemical biosensors and breast cancer miRNA biomarkers were the main search terms utilized, along with early-detection-related keywords. Studies were chosen for the search based on their applicability to the subject. MicroRNAs, including miR-21, miR-155, and miR-122, are effective biomarkers for breast cancer linked to tumor development and metastasis. Electrochemical biosensors, enhanced by nanotechnology, detect these miRNAs with high sensitivity and selectivity. Utilizing gold nanoparticles and graphene oxide, these biosensors enable real-time and portable diagnostics, enhancing their potential in point-of-care settings. Electrochemical biosensors based on miRNA biomarkers show promise for the early detection of breast cancer due to their high sensitivity, selectivity, and cost-effectiveness. Further research is necessary to validate their clinical efficacy and develop standardized protocols. Clinicians should stay informed about these advancements to potentially integrate them into practice, improving patient outcomes.

Keywords:
Breast cancer, Biomarker, Biosensors, Diagnose, miRNAs

1. INTRODUCTION

In 2016, it was estimated that over 18 million people had cancer, and the disease was responsible for about 9.6 million fatalities. Metastasis is a major cause of cancer-related fatalities. Breast cancer, a diverse disease with an increasing global incidence, is one of the most common malignant tumors that endanger women's health [1]. Despite ongoing medical advancements, breast cancer (BC) remains the second most prevalent and fatal form of cancer in women. Over the past 40 years, there has been a concerning rise in its incidence. Approximately 700,000 people died from BC in 2020, and there were about 2.3 million new cases identified worldwide [2]. Because conventional diagnostic methods such as

---

* Corresponding author:

Solmaz Kia; E-mail: s.kia@uma.ac.ir

imaging mammography, ultrasound, magnetic resonance imaging, histology, and clinical and physical tests are inadequate, early detection of breast cancer is essential. Due to their low sensitivity, these techniques can expose users to radiation and provide false positive results. Despite being non-invasive, ultrasound cannot take the place of mammograms, particularly in women over 40 [3]. However, the patient may sustain invasive or radioactive harm as a result of these procedures. Furthermore, it is challenging to detect the formation of cancer using the aforementioned techniques if the tumor tissue lacks typical pathological abnormalities. With its simplicity, speed, non-invasiveness, and real-time capabilities, liquid biopsy is regarded as the most promising new detection tool for early cancer diagnosis [4]. Disease biomarkers and the associated detection techniques are two important aspects that have a direct impact on liquid biopsy performance [5]. Frequently, tumors are discovered after symptoms start to show. Early identification is typically associated with a better possibility of patient survival, making it a more advantageous course of action for cancer treatment. Therefore, the identification of chemicals produced in bodily fluids (such as blood, urine, and saliva) that can be obtained by minimally invasive or non-invasive procedures (such as liquid biopsy) is the foundation of next-generation cancer diagnostics. Liquid biopsies, in particular, can assist physicians in assessing the risk of metastatic relapse, monitoring therapy response in real time, and early screening patients for the best course of treatment. Among other things, liquid biopsy techniques focus especially on circulating nucleic acids, such as circulating tumor cells (CTCs), exosomes, and non-coding RNAs (ncRNAs). ncRNAs are increasingly being linked to cancer, making them intriguing epigenetic biomarker candidates for diagnosis and prognosis. MicroRNAs (miRNAs) and long non-coding RNAs (lncRNAs) are the two most significant and well-researched ncRNAs [6].

As a result, new biomarkers that are developing, such as miRNAs, in bodily fluids are crucial for breast cancer screening. A class of tiny endogenous non-coding RNAs known as miRNAs has been linked to several illnesses, including cancer. Because miRNAs are found in bodily fluids like blood, plasma, and serum, their use as a biomarker for cancer detection is crucial. Additional advantages of miRNAs as a biomarker include their stability at high temperatures, even at low or high pH levels, prolonged room temperature storage, and several freeze-thaw cycles [7]. The creation of biosensors with improved sensitivity, selectivity, stability, and cost has exploded in the last ten years. Based on their mode of detection and the kind of signal they produce; these sensors can be divided into several categories; the most widely used types are electrochemical and optical biosensors. Even if a lot of biosensors are still in the research and development stage, their eventual commercialization has enormous potential to increase the efficacy and efficiency of tumor marker detection in the diagnosis of breast cancer [8]. Because of their remarkable feature set, electrochemical biosensors have become a leading option for diagnosing breast cancer in this context. These sensors are small, inexpensive, have an easy-to-use design, great sensitivity, and efficient functioning [9]. They also have great potential to improve the sensitivity of biomarker detection. This is accomplished by using a variety of identification probes and cutting-edge materials, opening the door for novel approaches to breast cancer diagnosis and treatment [8].The most popular biosensing technique (BT) for measuring miRNA is the electrochemical nanobiosensor. It performs well when measuring a variety of substances, including proteins, enzymes, drugs, and miRNA [10]. This method uses the electrode as a converter and the biological element as a detecting component. Nanostructures are typically employed in this system to bridge the distance between the biological receiver and the converter. Nucleic acids, enzymes, bacteria, biological tissues, and antibodies that can immobilize on the electrode are examples of biological materials employed in nanobiosensors. Electrochemical techniques like potentiometric, amperometric, cyclic voltammetry, and impedance have been used to measure the electrical signal produced by the interaction between the analyte and biological element. Additionally, the analyte's concentration determines how strong this electrical signal is. Combining nanotechnology and the electrochemical biosensor creates a new area of BTs called the electrochemical nanobiosensor. Among the many diagnostic advantages of this approach is the easier, quicker, and less expensive access to proprietary data. Materials at the nanoscale improve the sensor's sensitivity, accuracy, and other characteristics while lowering the measurement limitations [11].Therefore, reducing mortality from breast cancer requires early detection. The use of biomarkers for early breast cancer detection is an intriguing area of research with significant promise to improve detection and treatment outcomes. Therefore, the use of biomarkers in early detection methods was reviewed in this article.[12].Thus, this review focuses on the recent progress in miRNA-based electrochemical biosensors for the early detection and monitoring of breast cancer. It aims to synthesize reported design strategies, nanomaterial integrations, and electrochemical approaches that enhance sensitivity, selectivity, and cost-effectiveness in liquid biopsy analysis. Furthermore, the study critically highlights current challenges such as clinical validation, reproducibility in real samples, and standardization, and outlines future research directions needed to facilitate the translation of these promising biosensing platforms into practical tools for personalized breast cancer diagnosis and management.

2. Objective

The document aims to explore the use of miRNA-based electrochemical biosensors for early detection of breast cancer, focusing on their reliability, sensitivity, selectivity, and affordability, and their potential to improve treatment outcomes, early diagnosis, and subtyping, thereby advancing personalized medicine.

3. Materials and Methods

Keywords and search strategy—In December 2025, a thorough search was carried out in PUBMED, Science Direct, ACS, Springerlink, Taylor & Francis, and Google Scholar using the selected keywords. Additionally, the following keywords were used in the search: electrochemical biosensors AND breast cancer AND miRNA breast cancer biomarker OR miRNA BC biomarkers AND early BC detection OR Breast Cancer Diagnosis.

4. Identification and Diagnosis of Breast Cancer

Breast cancer is the most common cancer among women globally, with mammography, ultrasonography, and imaging being the primary diagnostic methods. However, these tests are expensive due to specialized equipment and professional analysis. In recent years, electrochemical biosensors have been developed and successfully used in the detection of tumor biomarkers due to their high sensitivity and inexpensive equipment costs [13]. BC is a multifaceted illness with distinct subtypes like triple-negative (TN) and estrogen receptor-positive (ER+), each with unique risk factors and molecular fingerprints. Precise subtyping is crucial for understanding the disease's complexity and individualized treatment plans, but detecting multiple biomarkers is challenging [14]. Because aberrant expression of particular microRNAs and enzymes is directly linked to the formation and spread of cancer, early detection and identification of metastatic breast cancer are therefore essential for successful therapy [15].For breast cancer patients to receive effective therapy and have a good prognosis, early diagnosis is essential. The early detection of breast cancer and precise lesion diagnosis are the goals of imaging modalities. The two primary pillars of efficient illness management are early detection and timely treatment [16]. Breast imaging is critical for detecting, diagnosing, and controlling cancers. Ultrasound is a common medical technique, alongside positron emission tomography (PET), mammography, ultrasound, MRI, scintimammography, and single photon emission computed tomography (SPECT) [17]. The diagnosis and assessment of breast cancer establish whether preoperative systemic therapy is required. Effective, targeted therapies are essential. One of the main priorities is lowering worldwide disparities in diagnosis, care, and cutting-edge drugs [8].

4.1. Mammography

Mammography is a diagnostic technique that can be used for screening and diagnosis. It creates images of the breast using x-ray technology, identifying benign or malignant abnormalities [16]. By finding early signs of breast cancer, mammogram screening lowers mortality. However, automated methods are not enough to predict the occurrence of breast cancer. Increasing mammographic density can improve breast cancer risk models, and gold-based nanoformulations can improve the contrast of mammogram images [18].

4.2. MRI

Because early detection and treatment are essential for improved patient outcomes, the American Cancer Society (ACS) advises women with a lifetime risk of 20–25% or higher to undergo annual breast magnetic resonance imaging (MRI). Although MRI is more expensive, it is usually more sensitive and offers more thorough pathophysiology data. Breast MRI produces three-dimensional images utilizing radio waves and magnets, and it has an average cancer output of 22 malignancies per 1000 women screened. This is ten times higher than mammography and twice as high for high-risk women. For women who are genetically or familially at high risk, contrast-enhanced breast MRI has been verified [19].

4.3. Magnetic Resonance Spectroscopy

Because of its better sensitivity and negative predictive value, dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) is the gold standard for detecting breast cancer. Its specificity, though, may result in further diagnostic testing and needless biopsies. For supplemental lesion characterization, substitutes like diffusion-weighted imaging and magnetic resonance spectroscopy (MRS) have been suggested [20]. Diffusion-weighted imaging (DWI) is a technique that enhances the anatomical features of magnetic resonance imaging (MRI) by providing microstructural and functional information. Despite its high sensitivity for cancer detection, DWI has limitations, such as the need for gadolinium contrast agents and contraindications for certain groups. DWI

DOI: 10.30473/ijac.2026.77335.1342

uses the apparent diffusion coefficient (ADC) to distinguish between benign and malignant breast lesions. Recent developments in MRI gradient hardware allow for the study of time-dependent ADCs, making DWI a popular alternative for breast lesion assessment [21].

4.4. Magnetic Resonance Elastography

Magnetic resonance elastography (MRE) is a non-invasive imaging technique used to measure the viscoelastic characteristics of breast tissues under external stress. Breast tumors are often more rigid due to their higher cell, collagen, and proteoglycan content. MRE can help overcome the limitations of manual palpation in breast cancer screening, but its main limitation is its inability to detect small focal lesions and achieve spatial resolution due to overlap between benign and soft malignant tumors [16].

4.5. Sentinel Lymph Node Biopsy (SLNB)

Sentinel lymph node biopsy (SLNB) is the standard procedure for early breast cancer surgery, replacing axillary lymph node dissection (ALND) for clinically node-negative cases. SLNB is minimally invasive and yields the same staging information as ALND. Neo-adjuvant chemotherapy (NAC) is being studied to downstage the axilla in advanced loco-regional BC, reducing the need for axillary surgery and preventing ALND consequences [22].

4.6. Breast-Specific Gamma Imaging

Breast-specific gamma imaging (BSGI) is a molecular breast imaging technique similar to MRI, used to identify sub-centimeter and mammographically occult breast cancer. It uses a radiotracer like Technetium Tc99m Sestamibi and a specialized camera to view the breast. Breast density doesn't affect BSGI, unlike mammography. Compared to scintimammography, BSGI has higher sensitivity for detecting sub-centimeter lesions. However, it's not suitable for routine breast cancer screening due to radiation exposure [16]. Sonography, also known as ultrasound, is an imaging technique that uses sound waves to create images of internal body structures, providing crucial information for diagnosing various illnesses, and combining ultrasound and MRI enhances tumor identification precision [23]. Breast ultrasonography offers a significant advantage over mammography by using sound waves instead of ionizing radiation. X-rays are used in mammograms for accurate breast tissue images, but ionizing radiation exposure raises concerns, especially during multiple screenings, in younger age, and pregnant women. Breast ultrasonography uses safe sound waves, making it a safer choice for routine screenings [24].

4.7. Automated Breast Ultrasound (ABUS)

The automated breast volume scanner (ABVS) is unable to distinguish between benign and malignant tumors, so a 3D quasi-static elastography system was developed to analyze dense breast tissue. This system uses cross-model attention-guided tumor segmentation, achieving a precision of 74.51% and recall of 64.43% in ABUS images, overcoming the limitations of mammography [23]. Breast cancer imaging techniques face challenges like high costs and balancing sensitivity and specificity. New biomarkers are needed to detect and monitor breast cancer early and continuously, understand molecular processes, develop targeted treatments, and track patient reactions. Biochemical markers like proteins, mRNAs, enzymes, and microRNAs have shown promise [8]. According to the research reviewed above, while mammography and ultrasound are the most commonly used diagnostic techniques for breast cancer, newer modalities like DCE-MRI, MRE, SLNB, and BSGI are being considered for effective data collection. MRI can capture data from both breasts, while conventional mammography can only focus on one. Contrast agents can also enhance the quality of the data.

5. Biosensors and Breast Cancer

5.1. Biosensor-Based Clinical Diagnostics and Their Use in the Detection of Cancer

Biosensors are essential tools for cancer monitoring and diagnosis. They convert biological reactions into quantifiable data using a biological component like cells or macromolecules and a physicochemical detector. These devices offer high sensitivity, specificity, and speed of detection, making them useful for early detection, prognosis, and therapy monitoring. **(Fig. 1)** Technological developments are expected to enhance biosensor capabilities and applications in cancer diagnosis, particularly in breast cancer early detection. Biosensors hold great promise for the early detection of cancer [12].

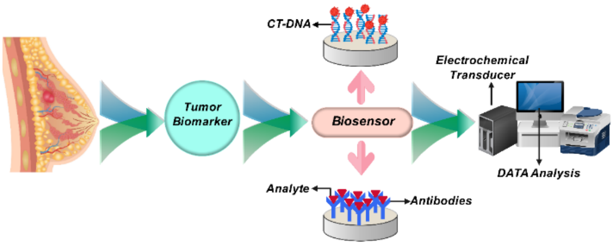

Fig. 1. Integrating engineering technologies in biosensor development can enhance the sensitivity and accuracy of cancer-specific biomarker detection for early detection [12].

5.2. Electrochemical Biosensors

Biosensors are analytical devices that detect target molecules, crucial for the early detection of breast cancer, molecular subtype categorization, therapeutic approach

DOI: 10.30473/ijac.2026.77335.1342

selection, and prognosis assessment. They offer advantages in specificity, sensitivity, speed, and cost compared to conventional methods. Over the past decade, numerous biosensors have improved in sensitivity, selectivity, stability, and affordability. This study reviews research on various types of biosensors, including optical and electrochemical biosensors, developed for identifying breast tumor indicators. Electrochemical biosensors detect target molecules by observing the electrochemical response on electrode surfaces. Cyclic voltammetry (CV), differential pulse voltammetry (DPV), square wave voltammetry (SWV), linear sweep voltammetry (LSV), electrochemical impedance spectroscopy (EIS), field-effect biosensors (FET), and other techniques are the primary techniques for electrochemical detection [25]. A biomarker is a feature that can be objectively measured and evaluated to indicate normal biological processes, pathological processes, or pharmacological responses to therapeutic interventions. These biomarkers can be found inside or outside cells and can be used to determine the course of breast cancer and differentiate between cancer patients and healthy individuals. Examples of potential biomarkers include cell surface receptor proteins, mutant genes, microRNAs, cells, and exosomes. A summary of the several kinds of biomarkers linked to breast cancer, such as altered genes and microRNAs, is shown in **Fig 2** [26].

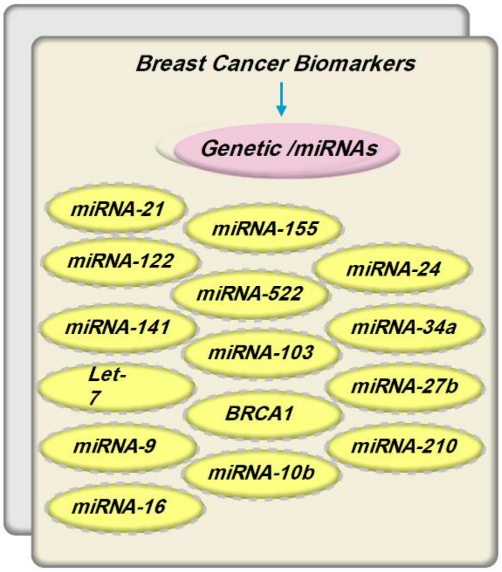

Fig 2. provides a comprehensive overview of various biomarkers linked to breast cancer, such as mutated genes and microRNAs [27-29].

Electrochemical biosensors efficiently detect miRNAs due to low detection limits, low equipment costs, and small sample volumes, enabling simultaneous detection of multiple analytes using DNA immobilization techniques [30]. Biosensor technologies are revolutionizing healthcare by enabling faster pathogen identification and simplifying disease response. They convert biological interactions into measurable signals using markers like proteins or glucose, eliminating centralized testing and enhancing disease outbreak response. These technologies can enhance breast cancer diagnostics by providing sensitive, specialized methods for early detection, personalized treatment, and improved patient outcomes[8].

5.3. Electrochemical Biosensors for Breast Cancer Diagnosis

Biomarkers, including proteins, molecules, DNA, microRNAs, and enzymes, are crucial for diagnosing and tracking breast cancer. Conventional methods have inadequate sensitivity, making early detection challenging. Electrochemical biosensors, which combine various identification probes and high-performance materials, improve biomarker detection sensitivity and offer new avenues for breast cancer surveillance [31]. Electrochemical biosensors, primarily immuno- and geno-sensors, are used to determine circulating breast cancer biomarkers. These bioreceptors include DNA/RNA strands, aptamers, antibodies, and peptides. Advances in screen-printed electrodes (SPEs), magnetic beads (MBs), and nanomaterials are improving analytical performance, miniaturization capability, and production costs. Genetic biomarkers used for non-invasive breast cancer diagnosis include detecting gene mutations and dysregulation of specific miRNAs [32]. A biosensor is an electronic device that aids in the early diagnosis of breast cancer by identifying and measuring BC biomarkers. It consists of a bio-receptor and transducer, converting recognition into a quantifiable signal. Electrochemical biosensors are cost-effective and simple, offering high sensitivity and selectivity. Performance is evaluated based on linear range, sensitivity, reaction time, limit of detection, selectivity, stability, and repeatability [33].

Nucleic acids are versatile and advantageous bio-receptors, capable of detecting and recognizing various analytes. They are used in biosensing for the detection and tracking of breast cancer, with electrochemical biosensors being integrated for diagnosis. These biosensors consist of probe DNA that self-hybridates onto the sensor surface, producing an electrochemical signal based on the concentration of the target biomarker. Nucleic acid-based compounds, such as aptamers, demonstrate selectivity, sensitivity, and binding capabilities to various targets, including proteins, metabolites, and whole cells. Recent developments in electrochemical biosensors based on aptamers have gained interest for cancer detection due to their mobility, disposability, and on-site analysis. These biosensors offer multiplexed monitoring, low cost, and noninvasive nature, allowing simultaneous assessment of multiple targets in a single drop of patient sample [34].

6. Biomarkers of BC

Tumor biomarker detections are crucial for diagnosing, tracking, classifying, evaluating chemotherapy resistance, and staging cancer.

Biosensors can be classified based on biorecognition substance and transducer type. Electrochemical biosensors, based on electrochemical interactions, enable the simultaneous estimation of multiple analytes with high sensitivity and specificity. The development of sensitive, robust, and selective biosensors for cancer diagnostics is promising due to low sample pre-treatment procedures. These platforms offer real-time evaluation and high sensitivity, making them ideal for portable use in patient care or doctor's offices [35].

6.1. MiRNAs are Detected and Measured Electrochemically

A significant portion of the human transcriptome is made up of noncoding RNAs (ncRNAs), a family of functional RNA molecules that lack the protein-coding characteristic. These include circular RNAs, transfer RNAs, ribosomal RNAs, long ncRNAs, and short ncRNAs. With lengths of roughly 20–25 nucleotides, microRNAs (miRNAs) are a highly conserved class of small noncoding RNAs that mainly control gene expression by either encouraging messenger RNA breakdown or suppressing its translation. Numerous human disorders, including cancer and immunological dysfunction, are linked to abnormal expression of miRNAs, which regulate a range of cellular processes involving development, differentiation, and signaling. Since miRNAs are soluble and detectable in cancer cells, blood, plasma, and patient saliva, they have drawn more interest as cancer biomarkers for the non-invasive early diagnosis, detection, and treatment of breast cancer [28]. Recent studies have used RNA extracted from patient biological materials, including mRNA and miRNA, to diagnose cancers. In **Table 1**, a collection of studies on the electrochemical detection of breast cancer biomarkers in nucleic acids in standard solutions is presented, using only analyte. Biosensors like colorimetry, fluorescence, and electrochemistry have been used to track miRNA-21 in bodily fluids. These studies show that miRNA-21 is a useful breast cancer biomarker for detection, with electrochemical biosensors showing high sensitivity and specificity for miRNA target analytes. MiRNAs are used as biological markers in various diseases, including cancer, viral infections, cardiovascular disorders, and metabolic disorders, due to their role in regulating physiological and pathological processes [36]. One of the specific microRNA markers linked to breast cancer is the overexpression of miR-21, which is associated with increased cell invasion and proliferation. Breast cancer development, especially triple-negative breast cancer, has been linked to elevated miR-155 levels. While miR-146a deregulation is linked to the development of breast cancer and plays a role in

Table 1. Selected research on the electroanalytical detection of breast cancer biomarkers in nucleic acid in standard solutions with just the analyte [28].

Biomarker Analyte	Redox Probe	Biosensor Design	Technique	LOD	Linear Range	Ref.
miR-122	$[Fe(II)(CN)_6]^{4-}/Fe(III)(CN)_6]^{3-}$	Au/Au NPs/rGO/SH-ssDNA	DPV	1.7×10^{-12} M	1.0×10^{-11}–1.0×10^{-5} M	[37]
	——	SPGE/ssDNA	DPV	5.0×10^{-9} M	——	[38]
miR-522	Os(VI)bipy	HDME/ssDNA	DPV	2.0×10^{-9}	2.0×10^{-9}–4.0×10^{-8} M	[39]
	Os(VI)bipy	HMDE/ssDNA-MB	DPV	—-	1.0×10^{-8}–2.0×10^{-7} M	[40]
miR-24	——	GCE/PANI-PA/ssDNA	DPV	3.4×10^{-16} M	1.0×10^{-15}–1.0×10^{-12} M	[41]
	Mb	GCE/MWCNT-PAMAM/ssDNA	DPV	5.0×10^{-16} M	1.0×10^{-14}–1.0×10^{-7} M	[42]
miR-34a	——	GO-PGE/ssDNA	DPV	(5.0×10^{-3} g L^{-1})	1.0×10^{-2}–4.0×10^{-2} g L^{-1}	[43]
	——	CA-IL-PGE/ssDNA	DPV	(8.8×10^{-4} g L^{-1}) (7.0×10^{-7} g L^{-1})	2.0×10^{-3}–10×10^{-2} g L^{-1}	[44]
	$[Co(phen)_3{}^{3+}]$	PGE/ssDNA	DPV	8.4×10^{-8} M 1.3×10^{-7} M	1.4×10^{-7}–4.3×10^{-7} M	[45]
miR-103	PbS-QDs, CdS-QDs	GCE; LCR, MB–CP1CP2; PbS-QDs, CdS-QDs	SWV	3.1×10^{-14} M	5.0×10^{-14} – 1.1×10^{-9} M	[46]
miR-27b	PbS-QDs, CdS-QDs	GCE; LCR, MB–CP1CP2; PbS-QDs, CdS-QDs	SWV	3.1×10^{-14} M	5.0×10^{-14} – 1.1×10^{-9} M	[47]
let-7	——	Au/GQ-DNA-CHA-hemin/GQ DNAzyme	DPV	4.6×10^{-16} M	1.0×10^{-15}–1.0×10^{-9} M	[48]
miR-141	——	GCE/poly(JUGco-JUGA)	SWV	6.5×10^{-13} M	5.0×10^{-13}–1.0×10^{-10} M	[49]
	HRP	Au/rGE/CNTs/ssDNA; ELISA-like amplification	SWV	1.0×10^{-14} M	1.0×10^{-14}–1.0×10^{-9} M	[50]
	Thi, Fc	Au/HCP1-HCP2, ssDNA1/Fe_3O_4 NPs/Thi, ssDNA2/Fe_3O_4 NPs/Fc, HCR	DPV	4.4×10^{-16} M	—-	[28]
miR-155	RSV	CPE/Fe_3O_4NPs@Ag/NH_2 -ssDNA	DPV	1.5×10^{-16} g/mL	5.0×10^{-16} – 1.0×10^{-9} g/mL	[51]
	OB	GCE/GO/Au NRs/SH-ssDNA	DPV	6.0×10^{-14} M	2.0×10^{-15}–8.0×10^{-12} M	[52]
	$PMo_{12}O_{40}{}^{3-}$	GCE/MWCNTs/PtNPs/DNA, CHA, PSC@Au NPs-ALP, NPP	DPV	1.6×10^{-15} M	1.0×10^{-14}–1.0×10^{-9} M	[53]

	hematoxylin	GCE/Fe-Ni@rGO/QD-Ag, Au NS/SH-ssDNA	DPV	2.0×10^{-17} M	5.0×10^{-20}– 5.0×10^{-11} M	[54]
	HRP	Au/ssDNA-GQDs	A	1.4×10^{-16} M	1.0×10^{-15}– 1.0×10^{-13} M	[50]
	Mb	Au/PNA21, PNA155—CHA	SWV	1.1×10^{-14} M	5.0×10^{-14}– 5.0×10^{-8} M	[55]
	PbS-QDs, CdS-QDs	GCE; LCR, MB–CP1CP2; PbS-QDs, CdS-QDs	SWV	1.2×10^{-14} M	5.0×10^{-14}– 3.0×10^{-11} M	[56]
miR-21	Fc	SPCE/rGOs/Au NPs/SH-ssDNA; Fc-Au NPs-ssDNA	DPV	5.0×10^{-15} M	1.0×10^{-14}– 2.0×10^{-12} M	[57]
	Fc	ITO/PET/hydrogel-ssDNA	DPV	5.0×10^{-9} M	1.0×10^{-8}– 5.0×10^{-5} M	[58]
	Fc	Au/PNA21, PNA155; Fc-CHA21, Mb-CHA155 detection	SWV	2.4×10^{-15} M	1.0×10^{-14}– 5.0×10^{-9} M	[55]
	Mb	Au/chitosan/ssDNA origami	DPV	8.0×10^{-14} M	1.0×10^{-13}– 1.0×10^{-8} M	[59]
	Mb	PGE/CB-Au NPs/ssDNA	DPV	1.0×10^{-15} M	2.9×10^{-15}– 7.0×10^{-7} M	[60]
	MDB	PGE/PPy/ssDNA	DPV	1.7×10^{-10} M	——	[61]
	Mb, TCEP	Au/LNA-TWJ	ACV	7.7×10^{-17} M	1.0×10^{-16}– 1.0×10^{-10} M	[62]
	TB	Au/Au NPs-PPy/ssDNA	DPV	7.8×10^{-17} M	1.0×10^{-16}– 1.0×10^{-9} M	[63]
	K_3 $[Fe(CN)_6]$, $[Ru(NH_3)_6]Cl_3$	SPCE/Au NPs/ssDNA	SWV	4.0×10^{-16} M	1.0×10^{-15}– 1.0×10^{-11} M	[64]
	Ag NPs	GCE/Au NPs/DNA	LSV	2.0×10^{-17} M	1.0×10^{-16}– 5.0×10^{-14} M.	[65]
	HRP	SPCE/Au NPs/ssDNA	SWV	1.9×10^{-14} M	1.9×10^{-5}– 1.0×10^{-1} M	[66]
	$[Fe(II)(CN)_6]^{4-}/Fe(III)(CN)_6]^{3-}$	GCE/SA/ssDNA	EIS	2.0×10^{-14} M	1.0×10^{-14}– 1.0×10^{-8} M	[67]
	$[Fe(II)(CN)_6]^{4-}/Fe(III)(CN)_6]^{3-}$	GCE/HP1, HP2, DG-TIS	DPV	3.5×10^{-14} M	5.0×10^{-14}– 5.0×10^{-7} M	[68]
	CeO2 -Au@GOx	μPAD/Au NRs	DPV	4.3×10^{-16} M	1.0×10^{-15}– 1.0×10^{-12} M	[69]
	MoS2-Thi-Au NPs	GCE/MoS2 -Thi-Au NPs/ssDNA	SWV	2.6×10^{-13} M	1.0×10^{-12}– 1.0×10^{-8} M	[70]
	—	Au/SWCNs/NDs/ssDNA-HCR-hemin/GQ DNAzyme	DPV	2.0×10^{-15} M	1.0×10^{-14}– 1.0×10^{-9} M	[71]
	Fc	GCE/rGO/β-CD/HP-DNAzyme	DPV	1.8×10^{-15} M	1.0×10^{-15}–1.0×10^{-10} M	[72]
	Thi, Fc	Au/HCP1-HCP2, ssDNA1/Fe3O4 NPs/Thi, ssDNA2/Fe3O4 NPs/Fc, HCR	DPV	4.6×10^{-16} M	—-	[56]

inflammation and carcinogenesis, miR-10b is linked to the invasive and metastatic potential of breast cancer cells, and miR-34a functions as a tumor suppressor, and low levels are associated with a poor prognosis in breast cancer. The expression profiles of these microRNAs, which are present in patient samples such as blood or tissue, can aid in the diagnosis and treatment of breast cancer. Research on microRNA biomarkers is ongoing and could potentially improve current diagnostic techniques [12].

Research has demonstrated that miR-199a-5p, a circulating miRNA, may be a good option for the early diagnosis of Triple Negative Breast Cancer (TNBC). A novel electrochemical nanobiosensor for serum miR-199a-5p detection was developed using graphene oxide and gold nanoroad. The electrochemical properties and behavior of the nanobiosensor were investigated using the electrochemical impedance method (EIS). The synthesis of nanomaterials was confirmed using scanning electron microscopy (SEM), field emission scanning electron microscopy (FE-SEM), UV-Vis spectrophotometry, and energy dispersive spectroscopy (EDS). The microRNA 199a-5p detecting electrochemical nanobiosensor was tested for the first time, offering a straightforward, easy-to-use, and reasonably priced approach for identifying and measuring target miRNA in human serum samples and FBS. The low detection limit indicates high sensitivity in detecting target miRNA. This nanobiosensor can be used to identify low levels of miR-199a-5p in early stages of TNBC [11].

MiR-122 is a crucial diagnostic marker in breast cancer screening, diagnosis, and treatment evaluations. Circulating miR-122 predicts metastases in patients and influences therapeutic approaches. Elevated blood levels of miR-122 are linked to metastases in BC patients. Blood tests can monitor treatment effectiveness.The PBA-AuMXene QD nanocomposite was used in the production of this miR-122 biosensor. By adding Au-MXene QD, PBA, a non-conductive polymer, could be converted into a conductive composite using this technique. Next, thiol-Au linkages were used to covalently fix the thiolated ssDNA probe to the nanocomposite surface. The creation of an ultrasensitive biosensor to identify the breast cancer biomarker miR122 is described in this work. The biosensor had a broad linear diagnostic range, low LOD, and good sensitivity for miR-122 detection [73].

The biosensor uses a Metal-Organic Framework (MOF) structure and magnetic rod carbon paste electrodes. It uses materials like Fe@rGO, CuBTC-AIA (CuMOF), and carbon nanofibers to improve electrode surface-to-volume ratio and speed up electron transfer. MicroRNAs are attached to the electrode surface using 1-pyrenebutyric acid N-hydroxysuccinimide ester. Tests show selectivity and repeatability, and the nanobiosensor can detect microRNA 155 without interference. The MoSe2@1T-MoS2 heterojunction electrode material and specific RNA recognition probes are used [74]. Mir-155, a carcinogenic miRNA, is a key biomarker for cancer diagnosis, staging, progression, and prognosis. Its overexpression in breast cancer promotes tumorigenesis, and its concentration increases in patients' sera. The precise and accurate measurement of miR-155 in serum or plasma is crucial for early detection and prognosis of breast cancer, as it is a prominent circulating miRNA[52].

The study suggests that miRNA expression profiles could be valuable diagnostic indicators for breast cancer patients. MiRNAs like miR200c, miR-16, Let-7, miR-183, miR-34c, and miR-203 target key cellular and molecular pathways like Sp1, Wip1, EMT, and BMI1. These findings highlight the critical roles of various miRNAs in breast cancer development and metastasis, suggesting that using these miRNAs as therapeutic and diagnostic biomarkers could improve patient care[8].

7. Discussion

The review emphasizes the importance of early breast cancer diagnosis and the potential of electrochemical biosensors using miRNAs as a viable strategy. It acknowledges the drawbacks of conventional techniques like MRI and mammography, which often have low sensitivity and radiation exposure. MiRNAs like miR-21 and miR-155 are used as stable biomarkers in liquid biopsy for cancer diagnosis [75]. This review focuses on electrochemical biosensors, particularly those with nanotechnology, which enhance sensitivity and reduce detection limits. It contrasts with optical biosensors and other techniques, such as differential pulse voltammetry. The review highlights unique designs like graphene oxide and gold nanorods for certain miRNAs and highlights the multiplexed detection of numerous miRNAs, a recent development compared to single biomarkers. Biosensors could be used in personalized medicine to subtype breast cancer and monitor therapy response in real time, aligning with the field's direction and providing insights into specific advancements and their potential impact on treatment outcomes [8].

The analysis of current biosensing platforms for breast cancer highlights electrochemical biosensors as highly promising tools for miRNA detection, due to their high analytical sensitivity, low cost, and suitability for point-of-care applications [76; 77].Compared with optical methods, electrochemical systems offer advantages in miniaturization and lower background interference, particularly in liquid biopsy applications [78].Furthermore, integration with nanostructured materials such as graphene derivatives, MXenes and metal organic frameworks markedly enhances electron transfer kinetics and signal amplification, enabling ultrasensitive detection of target miRNAs. Nevertheless, important limitations persist, including susceptibility to biofouling in complex biological matrices, batch-to-batch variability, and insufficient large-cohort clinical validation [79] Optical biosensors, although generally more instrument-dependent and costly, still provide strengths in multiplex imaging capability and label-free detection in certain analytical contexts.Therefore, future progress in miRNA biosensing for breast cancer will depend on rigorous platform benchmarking, antifouling interface engineering, standardized fabrication protocols, and comprehensive clinical validation to facilitate clinical translation.[78; 79]

8. CONCLUSIONS

This review demonstrates that miRNA-based electrochemical biosensors are emerging as powerful tools for the early detection and monitoring of breast cancer, offering clear advantages over conventional diagnostic approaches in terms of sensitivity, miniaturization, cost, and suitability for liquid biopsy. The literature consistently shows that integrating advanced nanomaterials, efficient probe immobilization strategies, and antifouling interfaces markedly improves analytical performance, enabling ultrasensitive detection of clinically relevant miRNAs such as miR-21, miR-155, miR-199a-5p, and miR-122.

However, critical gaps remain between laboratory success and clinical implementation. Most reported platforms are validated in controlled conditions or limited sample sets, and challenges persist regarding standardization, reproducibility in complex biological matrices, long-term stability, and scalable manufacturing. In addition, the biological heterogeneity of breast cancer indicates that future progress will depend on multiplex miRNA panels rather than single-biomarker assays. Looking forward, research should prioritize large-cohort clinical validation, integrated point-of-care device development, and robust benchmarking frameworks. Addressing these issues will be essential for translating electrochemical miRNA biosensors from promising prototypes into clinically reliable tools. With continued interdisciplinary advances, these platforms have strong potential to complement existing screening methods and support more precise, personalized breast cancer management.

Acknowledgment

There is no acknowledgment in this manuscript.

REFERENCES

[1] A. J. Khameneh, S. Rahimi, M. H. Abbas, S. Rahimi, S. Mehmandoust, A. Rastgoo, A. Heydarian & V. Eskandari, Trends in electrochemical biosensors for the early diagnosis of breast cancer through the detection of relevant biomarkers. *Chemical Physics Impact*, *8*, (2024)100425. https://doi.org/10.1016/j.chphi.2023.100425

[2] A. Raucci, W. Cimmino, S. P. Grosso, N. Normanno, A. Giordano, & S. Cinti, based screen-printed electrode to detect miRNA-652 associated to triple-negative breast cancer. *Electrochimica Acta*, *487*, (2024) 144205. https://doi.org/10.1016/j.electacta.2024.144205

[3]A. R. Cardoso, F. T. Moreira, R. Fernandes & M. G. F. Sales, Novel and simple electrochemical biosensor monitoring attomolar levels of miRNA-155 in breast cancer. *Biosensors and Bioelectronics*, *80*, (2016) 621-630. https://doi.org/10.1016/j.bios.2016.02.035

[4] X. Xiao, L. Tang, C. Li, Z. Sun, Q. Yao, G.-j. Zhang, Y. Sun, F. Zhu & Y. Zhang, Cascade CRISPR/Cas12a and DSN for the electrochemical biosensing of miR-1246 in BC-derived exosomes. *Bioelectrochemistry (Amsterdam, Netherlands)*, *159*, (2024) 108753. https://doi.org/10.1016/j.bioelechem.2024.108753

[5] A. M. Shbeer, & I. A. Robadi, liquid biopsy holds a promising approach for the early detection of cancer: Current information and future perspectives. *Pathology-Research and Practice*, *254*, (2024). 155082. https://doi.org/10.1016/j.prp.2023.155082

[6] P. S. Sfragano, S. Pillozzi & I. Palchetti, Electrochemical and PEC platforms for miRNA and other epigenetic markers of cancer diseases: Recent updates. *Electrochemistry Communications*, *124*, (2021) 106929. https://doi.org/10.1016/j.elecom.2021.106929

[7] F. Hakimian, & H. Ghourchian, Ultrasensitive electrochemical biosensor for detection of microRNA-155 as a breast cancer risk factor. *Analytica Chimica Acta*, *1136*, (2020). 1-8. https://doi.org/10.1016/j.aca.2020.08.039

[8]P. Kiani, H. Vatankhahan, A. Zare-Hoseinabadi, F. Ferdosi, S. Ehtiati, P. Heidari, Z. Dorostgou, A. Movahedpour, A. Baktash & M. Rajabivahid, Electrochemical biosensors for early detection of breast cancer. *Clinica Chimica Acta*, (2024) 119923. https://doi.org/10.1016/j.cca.2024.119923

[9] M. Azimi Sanavi, F. Mahdavian, N. Dorosti, N. Karami, S. Karami, S. H. Khatami, O. Vakili, M. Taheri- Anganeh, S. Karima, & A. Movahedpour, A review of highly sensitive electrochemical genosensors for microRNA detection: A novel diagnostic platform for neurodegenerative diseases diagnostics. *Biotechnology and Applied Biochemistry*, *70*(3), (2023) 1044-1056. https://doi.org/10.1002/bab.2419

[10]H. Karimi-Maleh, F. Tahernejad-Javazmi, N. Atar, M. L. t. Yola, V. K. Gupta, & A. Ensafi, A novel DNA biosensor based on a pencil graphite electrode modified with polypyrrole/functionalized multiwalled carbon nanotubes for determination of 6-mercaptopurine anticancer drug. *Industrial & Engineering Chemistry Research*, *54*(14), (2015). 3634-3639. https://doi.org/10.1021/ie504438z

[11] A. Ebrahimi, I. Nikokar, M. Zokaei, & E. Bozorgzadeh, Design, development and evaluation of microRNA-199a-5p detecting electrochemical nanobiosensor with diagnostic application in Triple Negative Breast Cancer. *Talanta*, *189*, (2018) 592-598. https://doi.org/10.1016/j.talanta.2018.07.016

[12] M. R. A. Wahab, T. Palaniyandi, S. Viswanathan, G. Baskar, H. Surendran, S. Gangadharan, A. Sugumaran, A. Sivaji, S. Kaliamoorthy & S. Kumarasamy, Biomarker-specific biosensors revolutionise breast cancer diagnosis. *Clinica Chimica Acta*, *555*, (2024). 117792.

[13] D. Li, H. Wei, R. Hong, X. Yue, L. Dong, K. Fan, J. Yu, D. Yao, H. Xu & J. Lu, WS2 nanosheets-based electrochemical biosensor

for highly sensitive detection of tumor marker miRNA-4484. *Talanta*, *274*, (2024) 125965. https://doi.org/10.1016/j.talanta.2024.125965

[14] L. Mo, M. Mo, C. Yang & W. Lin, Enhancing RNA detection and breast cancer subtyping with a universal 3D-hybridization chain reaction system. *Talanta*, *277*, (2024). 126387. https://doi.org/10.1016/j.talanta.2024.126387

[15] Z. Ye, M. Ma, Y. Chen, R. Liu, Y. Zhang, P. Ma, & D. Song, Dual-microRNA-controlled electrochemiluminescence biosensor for breast cancer diagnosis and supplemental identification of breast cancer metastasis. *Analytical Chemistry*, *96*(8), (2024) 3636-3644. https://doi.org/10.1021/acs.analchem.3c05766

[16] A. Bhushan, A. Gonsalves & J. U. Menon, Current state of breast cancer diagnosis, treatment, and theranostics. *Pharmaceutics*, *13*(5), (2021). 723. https://doi.org/10.3390/pharmaceutics13050723

[17] H. Zhong, C. Zhao, J. Chen, M. Chen, T. Luo, W. Tang & J. Liu, Electrochemical immunosensor with surface-confined probe for sensitive and reagentless detection of breast cancer biomarker. *RSC advances*, *10*(38), (2020) 22291-22296. https://doi.org/10.1039/D0RA01192D

[18]A. Yala, C. Lehman, T. Schuster, T. Portnoi & R. Barzilay, A deep learning mammography-based model for improved breast cancer risk prediction. *Radiology*, *292*(1), (2019) 60-66. https://doi.org/10.1148/radiol.2019182716

[19] R. Adam, K. Dell'Aquila, L. Hodges, T. Maldjian & T. Q. Duong, Deep learning applications to breast cancer detection by magnetic resonance imaging: a literature review. *Breast Cancer Research*, *25*(1), (2023) 87. https://doi.org/10.1186/s13058-023-01687-4

[20] N. Nissan, A. Kulpanovich, R. Agassi, T. Allweis, I. Haas, E. Carmon, E. Furman-Haran, D. Anaby, M. Sklair-Levy, & A. Tal, Probing lipids relaxation times in breast cancer using magnetic resonance spectroscopic fingerprinting. *European Radiology*, *33*(5), (2023). 3744-3753. https://doi.org/10.1007/s00330-023-09560-w

[21] M. Iima, M. Kataoka, M. Honda, & D. Le Bihan, Diffusion-weighted MRI for the assessment of molecular prognostic biomarkers in breast cancer. *Korean Journal of Radiology*, *25*(7), (2024) 623. https://doi.org/10.3348/kjr.2023.1188

[22] C. Tinterri, A. Sagona, E. Barbieri, S. Di Maria Grimaldi, G. Caraceni, G. Ambrogi, F. Jacobs, E. Biondi, L. Scardina, & D. Gentile, Sentinel lymph node biopsy in breast cancer patients undergoing neo-adjuvant chemotherapy: clinical experience with node-negative and node-positive disease prior to systemic therapy. *Cancers*, *15*(6), (2023). 1719. https://doi.org/10.3390/cancers15061719

[23] S. Sushanki, A. K. Bhandari, & A. K. Singh, A review on computational methods for breast cancer detection in ultrasound images using multi-image modalities. *Archives of Computational Methods in Engineering*, *31*(3), (2024) 1277-1296. https://doi.org/10.1007/s11831-023-10015-0

[24] R. Iacob, E. R. Iacob, E. R. Stoicescu, D. M. Ghenciu, D. M. Cocolea, A. Constantinescu, L. A. Ghenciu, & D. L. Manolescu, Evaluating the role of breast ultrasound in early detection of breast cancer in low-and middle-income countries: a comprehensive narrative review. *Bioengineering*, *11*(3), . (2024) 262. https://doi.org/10.3390/bioengineering11030262

[25]R. Hong, H. Sun, D. Li, W. Yang, K. Fan, C. Liu, L. Dong, & G. Wang, A review of biosensors for detecting tumor markers in breast cancer. *Life*, *12*(3), . (2022) 342. https://doi.org/10.3390/life12030342

[26] Y.Deng, Y. Zhang, M. Zhou, B. Wu & J. Zhou, Application of Biosensors in Detecting Breast Cancer Metastasis. *Sensors*, *23*(21), . (2023) 8813. https://doi.org/10.3390/s23218813

[27] S. Sornambikai, H. Amir, G. Bhuvaneshwari, N. Ponpandian & C. Viswanathan, systematic review on electrochemical biosensing of breast cancer miRNAs to develop alternative DCIS diagnostic tool. *ECS Sensors Plus*, *1*(2), (2022) 021602.

[28] A.-M. Chiorcea-Paquim, Advances in electrochemical biosensor technologies for the detection of nucleic acid breast cancer biomarkers. *Sensors*, *23*(8), (2023). 4128.

[29]I. M. Mostafa, Y. Tian, S. Anjum, S. Hanif, M. Hosseini, B. Lou, & G. Xu, Comprehensive review on the electrochemical biosensors of different

breast cancer biomarkers. *Sensors and Actuators B: Chemical*, *365*, (2022) 131944.

[30] L. Hansen, S. N. Nagdeve, B. Suganthan, & R. P. Ramasamy, An Electrochemical Nucleic Acid Biosensor for Triple-Negative Breast Cancer Biomarker Detection. *Sensors*, *24*(17), (2024) 5747. https://doi.org/10.3390/s24175747

[31] Y. Zhang, S. Chen, X. Sun, H. Jing, & X. Zhou, Electrochemical biosensors for the non-invasive diagnosis of breast cancer. *Electrochimica Acta*, *468*, . (2023) 143190. https://doi.org/10.1016/j.electacta.2023.143190

[32] S. Campuzano, M. Pedrero & J. M. Pingarrón, (2017). Non-invasive breast cancer diagnosis through electrochemical biosensing at different molecular levels. *Sensors*, *17*(9), 1993. https://doi.org/10.3390/s17091993

[33]A. Mohammadpour-Haratbar, S. B. A. Boraei, Y. Zare, K. Y. Rhee & S.-J. Park, (2023). Graphene-based electrochemical biosensors for breast cancer detection. *Biosensors*, *13*(1), 80. https://doi.org/10.3390/bios13010080

[34] O. Gamal, M. H. Eldin, A. Refaat & R. Y. Hassan, Advances in nanocomposites-based electrochemical biosensors for the early diagnosis of breast cancer. *Frontiers in Sensors*, *5*, (2024) 1399441. https://doi.org/10.3389/fsens.2024.1399441

[35] C. J. Vellan, T. Islam, S. de Silva, N. A. M. Taib, G. Prasanna & J. Jayapalan, Exploring novel protein-based biomarkers for advancing breast cancer diagnosis: A review. *Clinical Biochemistry*, (2024) 110776. https://doi.org/10.1016/j.clinbiochem.2024.110776

[36]R. Salahandish, A. Ghaffarinejad, E. Omidinia, H. Zargartalebi, K. Majidzadeh-A, S. M. Naghib, & A. Sanati-Nezhad, Label-free ultrasensitive detection of breast cancer miRNA-21 biomarker employing electrochemical nano-genosensor based on sandwiched AgNPs in PANI and N-doped graphene. *Biosensors and Bioelectronics*, *120*, (2018) 129-136. https://doi.org/10.1016/j.bios.2018.08.025

[37] S. Kasturi, Y. Eom, S. R. Torati, & C. Kim, Highly sensitive electrochemical biosensor based on naturally reduced rGO/Au nanocomposite for the detection of miRNA-122 biomarker. *Journal of Industrial and Engineering Chemistry*, *93*, (2021) 186-195. https://doi.org/10.1016/j.jiec.2020.09.022

[38] E. Lusi, M. Passamano, P. Guarascio, A. Scarpa, & L. Schiavo, Innovative electrochemical approach for an early detection of microRNAs. *Analytical Chemistry*, *81*(7), (2009) 2819-2822. https://doi.org/10.1021/ac8026788

[39] M. Bartosik, M. Trefulka, R. Hrstka, B. Vojtesek & E.Palecek, Os (VI) bipy-based electrochemical assay for detection of specific microRNAs as potential cancer biomarkers. *Electrochemistry Communications*, *33*, (2013) 55-58. https://doi.org/10.1016/j.elecom.2013.04.009

[40]M. Bartosik, R. Hrstka, E. Palecek, & B. Vojtesek, Magnetic bead-based hybridization assay for electrochemical detection of microRNA. *Analytica Chimica Acta*, *813*, (2014) 35-40. https://doi.org/10.1016/j.aca.2014.01.023

[41] L. Yang, H. Wang, H. Lü & N. Hui, Phytic acid functionalized antifouling conducting polymer hydrogel for electrochemical detection of microRNA. *Analytica Chimica Acta*, *1124*, (2020) 104-112. https://doi.org/10.1016/j.aca.2020.05.025

[42] F. Li, J. Peng, Q. Zheng, X. Guo, H. Tang, & S. Yao, Carbon nanotube-polyamidoamine dendrimer hybrid-modified electrodes for highly sensitive electrochemical detection of microRNA24. *Analytical Chemistry*, *87*(9), (2015) 4806-4813. https://doi.org/10.1021/acs.analchem.5b00093

[43] E. Eksin, & A. Erdem, Electrochemical detection of microRNAs by graphene oxide modified disposable graphite electrodes. *Journal of Electroanalytical Chemistry*, *810*, (2018) 232-238. https://doi.org/10.1016/j.jelechem.2018.01.015

[44] E. Yaralı, E. Kanat, Y. Erac, & A. Erdem, Ionic liquid modified single- use electrode developed for voltammetric detection of miRNA- 34a and its application to real samples. *Electroanalysis*, *32*(2), (2020) 384-393. https://doi.org/10.1002/elan.201900353

[45] A. Erdem, E. Eksin, G. Kadikoylu & E. Yildiz, Voltammetric detection of miRNA hybridization based on electroactive indicator-cobalt phenanthroline. *International Journal of Biological Macromolecules*, *158*, (2020) 819-825. https://doi.org/10.1016/j.ijbiomac.2020.04.168

[46] H. V. Tran, N. D. Nguyen, B. Piro & L. T. Tran, Fabrication of a quinone containing layer on gold nanoparticles directed to a label-free and reagentless electrochemical miRNA sensor. *Analytical Methods*, *9*(18), (2017)

2696-2702. https://doi.org/10.1039/C7AY00665A

[47] W. Zhu, X. Su, X. Gao, Z. Dai & X. Zou, A label-free and PCR-free electrochemical assay for multiplexed microRNA profiles by ligase chain reaction coupling with quantum dots barcodes. *Biosensors and Bioelectronics*, *53*, (2014) 414-419. https://doi.org/10.1016/j.bios.2013.10.023

[48] R. Ren, Q. Bi, R. Yuan & Y.Xiang, An efficient, label-free and sensitive electrochemical microRNA sensor based on target-initiated catalytic hairpin assembly of trivalent DNAzyme junctions. *Sensors and Actuators B: Chemical*, *304*, (2020) 127068. https://doi.org/10.1016/j.snb.2019.127068

[49] H. Tran, B. Piro, S. Reisberg, G. Anquetin, H. Duc & M. Pham, An innovative strategy for direct electrochemical detection of microRNA biomarkers. *Analytical and Bioanalytical Chemistry*, *406*, (2014) 1241-1244. https://doi.org/10.1007/s00216-013-7292-4

[50] H. Tran, B. Piro, S. Reisberg, L. H. Nguyen, T. D. Nguyen, H. Duc, & M. Pham, An electrochemical ELISA-like immunosensor for miRNAs detection based on screen-printed gold electrodes modified with reduced graphene oxide and carbon nanotubes. *Biosensors and Bioelectronics*, *62*, (2014) 25-30. https://doi.org/10.1016/j.bios.2014.06.014

[51] S. Yazdanparast, A. Benvidi, M. Azimzadeh, M. D. Tezerjani, & M. R. Ghaani, Experimental and theoretical study for miR-155 detection through resveratrol interaction with nucleic acids using magnetic core-shell nanoparticles. *Microchimica Acta*, *187*, (2020) 1-10. https://doi.org/10.1007/s00604-020-04447-9

[52] M. Azimzadeh, M. Rahaie, N. Nasirizadeh, K., Ashtari & H. Naderi-Manesh, An electrochemical nanobiosensor for plasma miRNA-155, based on graphene oxide and gold nanorod, for early detection of breast cancer. *Biosensors and Bioelectronics*, *77*, (2016) 99-106. https://doi.org/10.1016/j.bios.2015.09.020

[53] W., Cai, S. Xie, Y. Tang, Y. Chai, R. Yuan & J. Zhang, A label-free electrochemical biosensor for microRNA detection based on catalytic hairpin assembly and in situ formation of molybdophosphate. *Talanta*, *163*, (2017) 65-71. https://doi.org/10.1016/j.talanta.2016.10.086

[54] F. Khosravi, M. Rahaie, M. R. Ghaani, M. Azimzadeh, & E. Mostafavi, Ultrasensitive electrochemical miR-155 nanocomposite biosensor based on functionalized/conjugated graphene materials and gold nanostars. *Sensors and Actuators B: Chemical*, *375*, (2023) 132877. https://doi.org/10.1016/j.snb.2022.132877

[55] P. Fu, S. Xing, M. Xu, Y. Zhao, & C. Zhao, Peptide nucleic acid-based electrochemical biosensor for simultaneous detection of multiple microRNAs from cancer cells with catalytic hairpin assembly amplification. *Sensors and Actuators B: Chemical*, *305*, (2020) 127545. https://doi.org/10.1016/j.snb.2019.127545

[56]Y.-H. Yuan, Y.-D. Wu, B.-Z. Chi, S.-H. Wen, R.-P. Liang, & J.-D. Qiu, simultaneously electrochemical detection of microRNAs based on multifunctional magnetic nanoparticles probe coupling with hybridization chain reaction. *Biosensors and Bioelectronics*, *97*, (2017) 325-331. https://doi.org/10.1016/j.bios.2017.06.022

[57] M. Zouari, S. Campuzano, J. M. Pingarrón, & N. Raouafi, Femtomolar direct voltammetric determination of circulating miRNAs in sera of cancer patients using an enzymeless biosensor. *Analytica Chimica Acta*, 1104, (2020) 188-198. https://doi.org/10.1016/j.aca.2020.01.016

[58] S. Liu, W. Su, Y. Li, L. Zhang, & X. Ding, Manufacturing of an electrochemical biosensing platform based on hybrid DNA hydrogel: Taking lung cancer-specific miR-21 as an example. *Biosensors and Bioelectronics*, *103*, (2018) 1-5. https://doi.org/10.1016/j.bios.2017.12.021

[59] S. Han, W. Liu, S. Yang & R. Wang, Facile and label-free electrochemical biosensors for microRNA detection based on DNA origami nanostructures. *ACS omega*, *4*(6), (2019) 11025-11031. https://doi.org/10.1021/acsomega.9b01166

[60]G. Yammouri, H. Mohammadi, & A. Amine, A highly sensitive electrochemical biosensor based on carbon black and gold nanoparticles modified pencil graphite electrode for microRNA-21 detection. *Chemistry Africa*, *2*, (2019) 291-300. https://doi.org/10.1007/s42250-019-00058-x

[61] M. Kaplan, T. Kilic, G. Guler, J. Mandli, A. Amine, & M. Ozsoz, A novel method for sensitive microRNA detection: Electropolymerization based doping. *Biosensors and Bioelectronics*, *92*, (2017) 770-778. https://doi.org/10.1016/j.bios.2016.09.050

[62] Z. Hu, B. Zhao, P. Miao, X. Hou, F. Xing, Y. Chen, & L. Feng, Three-way junction DNA

based electrochemical biosensor for microRNAs detection with distinguishable locked nucleic acid recognition and redox cycling signal amplification. *Journal of Electroanalytical Chemistry*, *880*, (2021) 114861. https://doi.org/10.1016/j.jelechem.2020.114861

[63] L. Tian, K. Qian, J. Qi, Q. Liu, C. Yao, W. Song, & Y. Wang, Gold nanoparticles superlattices assembly for electrochemical biosensor detection of microRNA-21. *Biosensors and Bioelectronics*, *99*, (2018) 564-570. https://doi.org/10.1016/j.bios.2017.08.035

[64] M. Labib, N. Khan, S. M. Ghobadloo, J. Cheng, J. P. Pezacki, & M. V. Berezovski, Three-mode electrochemical sensing of ultralow microRNA levels. *Journal of the American Chemical Society*, *135*(8), (2013) 3027-3038. https://doi.org/10.1021/ja308216z

[65] L. Liu, Y. Chang, N. Xia, P. Peng, L. Zhang, M. Jiang, J. Zhang, & L. Liu, Simple, sensitive and label–free electrochemical detection of microRNAs based on the in-situ formation of silver nanoparticles aggregates for signal amplification. *Biosensors and Bioelectronics*, *94*, (2017) 235-242. https://doi.org/10.1016/j.bios.2017.02.041

[66] R. Zayani, A. Rabti, S. B. Aoun, & N. Raouafi, Fluorescent and electrochemical bimodal bioplatform for femtomolar detection of microRNAs in blood sera. *Sensors and Actuators B: Chemical*, *327*, (2021) 128950. https://doi.org/10.1016/j.snb.2020.128950

[67] D. A. Smith, L. J. Newbury, G. Drago, T. Bowen, & J. E. Redman, Electrochemical detection of urinary microRNAs via sulfonamide-bound antisense hybridisation. *Sensors and Actuators B: Chemical*, *253*, (2017) 335-341. https://doi.org/10.1016/j.snb.2017.06.069

[68] C. Yan, J. Xu, L. Yang, B. Yao, G. Liu, & W. Chen, Target-triggered substantial stacking of electroactive indicators based on digestion-to-growth regulated tandem isothermal amplification for ultrasensitive miRNA determination. *Sensors and Actuators B: Chemical*, *344*, (2021) 130280. https://doi.org/10.1016/j.snb.2021.130280

[69] X. Sun, H. Wang, Y. Jian, F. Lan, L. Zhang, H. Liu, S. Ge, & J. Yu, Ultrasensitive microfluidic paper-based electrochemical/visual biosensor based on spherical-like cerium dioxide catalyst for miR-21 detection. *Biosensors and Bioelectronics*, *105*, (2018) 218-225. https://doi.org/10.1016/j.bios.2018.01.025

[70] D. Zhu, W. Liu, D. Zhao, Q. Hao, J. Li, J. Huang, J. Shi, J. Chao, S. Su, & L. Wang, Label-free electrochemical sensing platform for microRNA-21 detection using thionine and gold nanoparticles co-functionalized MoS2 nanosheet. *ACS applied materials & interfaces*, *9*(41), (2017) 35597-35603. https://doi.org/10.1021/acsami.7b11385

[71] L. Liu, C. Song, Z. Zhang, J. Yang, L. Zhou, X. Zhang, & G. Xie, Ultrasensitive electrochemical detection of microRNA-21 combining layered nanostructure of oxidized single- walled carbon nanotubes and nanodiamonds by hybridization chain reaction. *Biosensors and Bioelectronics*, *70*, . (2015) .351-357. https://doi.org/10.1016/j.bios.2015.03.051

[72] X. Lin, J. Jiang, J. Wang, J. Xia, R. Wang, & G. Diao, Competitive host-guest recognition initiated by DNAzyme-cleavage cycling for novel ratiometric electrochemical assay of miRNA-21. *Sensors and Actuators B: Chemical*, *333*, (2021) 129556. https://doi.org/10.1016/j.snb.2021.129556

[73]S. Ranjbari, B. Hatamluyi, S. H. Aghaee-Bakhtiari, M., Rezayi, & R. Arefinia, A label-free electrochemical biosensor based on PBA-Au-MXene QD for miR-122 detection in serum samples. *Microchimica Acta*, *190*(12), (2023) 482. https://doi.org/10.1007/s00604-023-06062-w

[74] E. A. Sadrabadi, A. Benvidi, M. Azimzadeh, L. Asgharnejad, A. S. Dezfuli, & P. Khashayar, Novel electrochemical biosensor for breast cancer detection, based on a nanocomposite of carbon nanofiber, metal–organic framework, and magnetic graphene oxide. *Bioelectrochemistry (Amsterdam, Netherlands)*, *155*, (2024) 108558. https://doi.org/10.1016/j.bioelechem.2023.108558

[75] P. S. Mitchell, R. K. Parkin, E. M. Kroh, B. R. Fritz, S. K. Wyman, E. L. Pogosova-Agadjanyan, A. Peterson, J. Noteboom, K. C. O'Briant, & A. Allen, Circulating microRNAs as stable blood-based markers for cancer detection. *Proceedings of the national academy of sciences*, *105*(30), (2008) 10513-10518. https://doi.org/10.1073pnas.0804549105

[76] M. Labib, N. Khan, & M. V. Berezovski, Protein electrocatalysis for direct sensing of circulating microRNAs. *Analytical Chemistry*, *87*(2), (2015) 1395-1403.

[77] M. El Aamri, G. Yammouri, H. Mohammadi, A. Amine & Korri-Youssoufi,

HElectrochemical biosensors for detection of microRNA as a cancer biomarker: Pros and cons. *Biosensors*, *10*(11), (2020) 186.

[78] L. Zhang, W. Su, S. Liu, C. Huang, B. Ghalandari, A. Divsalar & X. Ding, Recent progresses in electrochemical DNA biosensors for MicroRNA detection. *Phenomics*, *2*(1), (2022) 18-32.

[79] M. Labib, E. H. Sargent, & S. O. Kelley, Electrochemical methods for the analysis of clinically relevant biomolecules. *Chemical reviews*, *116*(16), (2016) 9001-9090

DOI: 10.30473/ijac.2026.77335.1342

زیست حسگر الکتروشیمیایی بر اساسmiRNA ها برای تشخیص زودهنگام سرطان سینه: یک بررسی جامع

الهام صاحبنظر[۱]، سولماز کیا[۲]*، سینا جعفری درگاهلو[۱]

۱- گروه بیوفیزیک، دانشکده فناوری‌های نوین، دانشگاه محقق اردبیلی، نمین، ایران.
۲- گروه علوم مهندسی، دانشکده فناوری‌های نوین، دانشگاه محقق اردبیلی، نمین، اردبیل

* E-mail: kia_solmaz@yahoo.com / s.kia@uma.ac.ir

تاریخ دریافت: ۲۲ مرداد ۱۴۰۴　　　تاریخ پذیرش: ۲۷ شهریور ۱۴۰۴

چکیده

سرطان سینه، که یک نگرانی مهم در حوزه سلامت جهانی است، در سال ۲۰۲۰ شاهد ۲٫۳ میلیون مورد جدید و ۷۰۰۰۰۰ مرگ گزارش شده است. روش‌های تشخیصی سنتی، مانند ماموگرافی، سونوگرافی و MRI، محدودیت‌هایی دارند که توسعه ابزارهای نوآورانه و غیرتهاجمی را ضروری می‌سازد. این مقاله به بررسی پتانسیل حسگرهای زیستی الکتروشیمیایی مبتنی بر miRNA برای تشخیص زودهنگام سرطان سینه می‌پردازد و بر قابلیت اطمینان، حساسیت، گزینش‌پذیری، مقرون‌به‌صرفه بودن و پزشکی شخصی‌سازی‌شده آنها تمرکز می‌کند. با استفاده از پایگاه‌های داده‌ای مانند PUBMED، Science Direct، ACS، Springerlink، Francis & Taylor و Google Scholar، جستجوی کاملی در متون در دسامبر ۲۰۲۵ انجام شد. حسگرهای زیستی الکتروشیمیایی و نشانگرهای زیستی miRNA سرطان سینه، همراه با کلمات کلیدی مرتبط با تشخیص زودهنگام، عبارات اصلی جستجو بودند. مطالعات بر اساس کاربرد آنها در موضوع، برای جستجو انتخاب شدند. میکرو RNAها، از جمله miR-21، miR-155 و miR-122، نشانگرهای زیستی مؤثری برای سرطان سینه مرتبط با توسعه تومور و متاستاز هستند. حسگرهای زیستی الکتروشیمیایی، که توسط فناوری نانو بهبود یافته‌اند، این miRNAها را با حساسیت و گزینش‌پذیری بالا شناسایی می‌کنند. این حسگرهای زیستی با استفاده از نانوذرات طلا و اکسید گرافن، امکان تشخیص در لحظه و قابل حمل را فراهم می‌کنند و پتانسیل کاربردی بودن آنها را در مراکز درمانی افزایش می‌دهند. حسگرهای زیستی الکتروشیمیایی مبتنی بر نشانگرهای زیستی miRNA به دلیل حساسیت، گزینش‌پذیری بالا و مقرون به صرفه بودن، نویدبخش تشخیص زودهنگام سرطان سینه هستند. تحقیقات بیشتر برای اعتبارسنجی اثربخشی بالینی آنها و توسعه پروتکل‌های استاندارد ضروری است. پزشکان باید از این پیشرفت‌ها مطلع باشند تا بتوانند آنها را به طور بالقوه در عمل ادغام کرده و نتایج درمان بیماری را بهبود بخشند.

کلید واژه ها

سرطان پستان, بیومارکر، زیست حسگر، تشخیص، miRNAs.

DOI: 10.30473/ijac.2026.77335.1342