Nanomaterial-Based Aptasensors

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Nanomaterial-Based aptasensors are used in rapid and accurate diagnosis of various biomarkers associated with medical conditions including early detection of viruses and bacteria.

aptamer gold nanoparticles quantum dots graphene MoS2 carbon nanotubes SELEX biomolecules diagnosis signal type limit of detection

1. Introduction

Rapid detection of small molecules is of great importance in medical and diagnostic fields, as this allows for early diagnosis of medical conditions. Traditional detection methods such as high-performance liquid chromatography (HPLC) coupled with mass spectrometry are time-consuming and require expensive equipment setup and preparation [1]. The multiplex immunoassay or capillary electrophoresis (CE) technique has the advantage of being fast and highly sensitive but there are setbacks regarding that described in [1]. One of the multiplex immunoassay techniques, enzyme-linked immunosorbent assay (ELISA) is commonly used to detect two or more classes of chemical (antibodies and antigens) simultaneously [2]. However, low antigenicity of small molecules has limited the application of ELISA because antibodies are less sensitive to small molecules [1][3][4]. Other types of biosensors such as surface plasmon resonance biosensor [5][6], polymerase chain reaction (PCR) [7], electrochemical sensors [8] are time-consuming because of complex samples and blood culture preparations [9].

The search for alternative recognition molecules has seen aptamers gain prominence due to their ability to detect and bind small molecules [3][10][11][12]. Aptamers, a suitable alternative to antibodies, are chemically derived single-stranded DNA (ssDNA) or RNA (ssRNA) with a high capability of folding into secondary or tertiary structures making them recognition molecules with high affinity and specificity to small molecules [1][11]. The possibility of generating aptamers in vitro, which have been pre-matched against target molecules using a synthetic library, has made them useful in early medical diagnosis. In addition, they can be cost effectively synthesized in large quantities and high purity via amplification of selected aptamers by polymerase chain reaction [11][13]. Moreover, the ease of chemical modification of aptamers including their stability at high temperature and pH can be utilized for optimized performance of various biosensor platforms (e.g., flow cytometry, electrochemical sensors, fluorescence microscopy, surface plasmon resonance sensor, or lateral flow assays) [14][15]. All these advantages have made aptamers a more robust biosensor than antibodies.

Research on aptamers has been on the increase, resulting in a steady rise in the number of publications from 2010–2021. The potential of aptamers as an alternative to antibodies in medical diagnosis has been established by various studies [15][16] and with ease of modification and stability, aptamers can be immobilized non-covalently to nanomaterials to produce biosensors with high specificity and selectivity. As a standalone, nanomaterials can be used as diagnostic devices due to their tunable physical, electrical and chemical properties but their inability to detect small molecules and their non-selectivity towards target biomolecule(s) has limited their adoption in medical diagnosis [17]. Conjugating aptamers with nanomaterials to produce high selective/sensitive biosensors (aptasensors) is now of great interest and importance in medical diagnostics and therapeutics due to their unique properties such as biocompatibility, tunable selectivity, low immune response [17]. Therefore, this review will focus mainly on improvement in aptamer selection via Systematic Evolution of Ligands by EXponential enrichment (SELEX) and the recent advances in fabricating aptamer–nanomaterial hybrids, and their applications as biosensors in Point-Of-Care (POC) diagnostics.

2. Nanomaterials Based Aptamer Sensors as Diagnostic Tool

Aptamers are chemically derived single strands of either DNA or RNA oligonucleotides that can be conjugated with various types of nanomaterials to produce POC aptasensors capable of detecting small molecules or biomarkers. In the conjugated device, the aptamer serves as a highly sensitive and selective recognition element while nanomaterials present high surface area and excellent optical, electrical and electrochemical properties rendering them as suitable and highly sensitive transducers [18][19]. The signals generated via the binding of small molecules by the aptasensors can be optical, colorimetric, electrochemical, fluorescence, surface-enhanced Raman spectroscopy/scattering (SERS), surface plasmon resonance (SPR) signals [20][21] and these types of signals are sometimes dependent on the nature and properties of the adjunct nanomaterials. A summary of application of nanomaterials as transducers in aptasensors and their dependency on types of detection signal is provided in Table 1.

Table 1. Summary of aptasensors based on commonly used nanomaterials.

Aptasensor	Signal Type	Target Molecule	Linear Range	Detection Limit	Reference
AuNPs-SEB aptamer	Colorimetry	Staphylococcal enterotoxin B	50 µg/mL–0.5 ng/mL	50 ng/mL	[22]
AuNPs-IL-6 aptamer	Colorimetry	Interleukin-6	3.3–125 µg/mL	1.95 µg/mL	[23]
AuNPs-thio/27-mer aptamer	Colorimetry	Thrombin	5 pM–2 nM	5 pM	[24]
AuNPs-$[Ru(NH_3)_6]^{3+}$-	Electrochemical	Thrombin	1 fM–6 pM	0.1429 fM	[25]

Aptasensor	Signal Type	Target Molecule	Linear Range	Detection Limit	Reference
TBA2 aptamer					
CDS-QDs/AuNPs/Tro6 aptamer	Electrochemiluminescence	Cardiac troponin 1	1 fg/mL–10 ng/mL	0.75 fg/mL	[26]
CdS-NCs/AuNPs/luminol aptamer	Ratiometric ECL	Thrombin	-	500 fg/mL	[27]
CDs/AS1411 aptamer	Spectrofluorometry	Cancer cells	-	~100 cells/mL	[28]
MoS_2-NS aptamer	Fluorescence	PSA		0.2 ng/mL	[29]
MoS_2-AuNPs/TiONBs/MC-LR aptamer	Electrochemical	Microcystin-LR	0.005–30 nM	0.002 nM6	[30]
SWCNTs-PBASE aptamer	FET	Capthepsin K	2.3 pM–0.23 nM	-	[31]
Graphene/SH-SAW aptamer	Surface Acoustic Wave	Endotoxins	0–100 ng/mL	3.53 ng/mL	[32]
GO/33-mer aptamer	Fluorescence	Theophylline	1–100 µM	0.155 µM	[33]
rGO-PET/cTnT aptamer	Electrical	Cardiac troponin T	0.001–10 ng/mL	1.2–1.7 pg/mL	[34]

3. Future Perspectives and Conclusions

The gradual rise in the application of biosensors in small molecule detection has made diagnosis and therapy of early onset of medical conditions an exciting possibility. Aptamer, an artificial single stranded DNA (ssDNA) or RNA (ssRNA) was synthesized due to limitations in antibodies' sensitivity to small molecules and complex setup of chromatographic detection methods. Since aptamers can be chemically synthesized and modified to detect specific biomarkers, they are now becoming the preferred tool for diagnosis of medical conditions. The selection protocol of these aptamers is based on SELEX which enables the isolation, purification, and amplification of target-binding oligonucleotides. However, the protocol could sometimes be actualized after 10–15 selection cycles and some improved methods were proposed with mixed results. The short half-lives of aptamers are a major challenge in biosensor industries. An improved performance in aptamers' selectivity and sensitivity is achieved upon conjugation with nanomaterials (aptasensor), which are themselves excellent sensing materials with tunable properties. At the same time, high sensitivity of nanomaterials can bring additional challenges; for instance,

tendency for self-agglomeration resulting in modulation of optical response. The aptasensors can bind small molecules with very low LOD ranging from nanomolar to femtomolar and the signals generated are dependent on the nature of the nanomaterials. Some research studies also confirmed the therapeutic potentials of aptasensors especially in inhibiting tumor growth but some of the setbacks include toxicity to human cells.

Due to technological advancement in nanomaterial synthesis and control, we foresee fabrication of aptasensors as portable medical devices that will be capable of detecting early biomarkers of disease condition and simultaneously be used as benign therapeutics.

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