Advancements and Challenges in Aptamer-Based Therapeutics and Diagnostics Across Diverse Medical Domains: A Comprehensive Review

Ahmed S.A. Ali Agha[1], Walhan Alshaer[2], Talal Aburjai[1*]

[1]Faculty of Pharmacy, Department of Pharmaceutical Sciences. The University of Jordan. Amman, Jordan.
[2]Cell Therapy Center, The University of Jordan, Amman, Jordan.

ABSTRACT

Aptamers, which are single-stranded DNA or RNA molecules, are increasingly recognized as important tools in diagnostics and therapeutics across various medical disciplines such as oncology, respiratory diseases, and neurological disorders. This review provides a comprehensive evaluation of the recent progress and obstacles encountered in the field of aptamer-based applications. Aptamers have shown promise in oncology for early cancer detection and targeted drug delivery, effectively reducing off-target effects. They also hold potential for significantly impacting the management of respiratory conditions such as asthma and Chronic Obstructive Pulmonary Disease (COPD) by selectively targeting cytokines and regulating the inflammatory response. In the realm of neurological disorders, aptamers offer novel methods by influencing the gut-brain axis and proposing potential approaches for early detection and specific therapy. Despite these notable benefits, persistent challenges remain in areas such as molecular stability, delivery mechanisms, and economic viability. This review offers a comprehensive overview of aptamer-based diagnostics and therapeutics while exploring potential avenues for future research.

Keywords: Aptamer Therapeutics, Diagnostic Aptamers, Immune Modulation, Mind-Gut Axis, Tumor-specific Markers.

INTRODUCTION

Aptamers have revolutionized molecular medicine, significantly impacting our approach to various health conditions. Aptamers show potential in disease diagnostics due to their precise target-binding capabilities [1], targeted therapies [2], and drug delivery [3]. This review explores a wide range of topics related to cancer [4], autoimmune diseases [5], metabolic dysfunctions [6], and mental well-being [7].

Aptamers have emerged as novel tools against cancer, a prevalent human health condition. The potential of precision diagnosis and targeted therapeutics [8-10] could offer promising prospects for enhancing the efficacy of cancer treatments. In autoimmune disorders, aptamers hold promise for facilitating more precise approaches to diagnosis and treatment.

Aptamers present a promising and innovative strategy for managing digestive disorders and metabolic dysfunctions. Their potential application in conditions such as malabsorption could lead to significant advancements in treatment methods [11], inflammatory bowel diseases [12], diabetes [13], and obesity [14].

Furthermore, aptamers play a crucial role in combating infectious diseases [15]. Significant progress has been made in the field of early detection and targeted treatments. Aptamers have also shown potential as therapeutic agents for promoting bone health, expanding their applications beyond traditional biomedical fields [16], and addressing psychological disorders [17].

[*]***Corresponding author: Talal Aburjai***
aburjai@ju.edu.jo
Received: 21/10/2023 Accepted: 30/1/2024.
DOI: https://doi.org/10.35516/jjps.v17i2.1895

This review highlights the various applications of aptamers, emphasizing their significant potential for advancements in health and medicine. It also anticipates a promising future impact by these molecules, as illustrated in Figure 1.

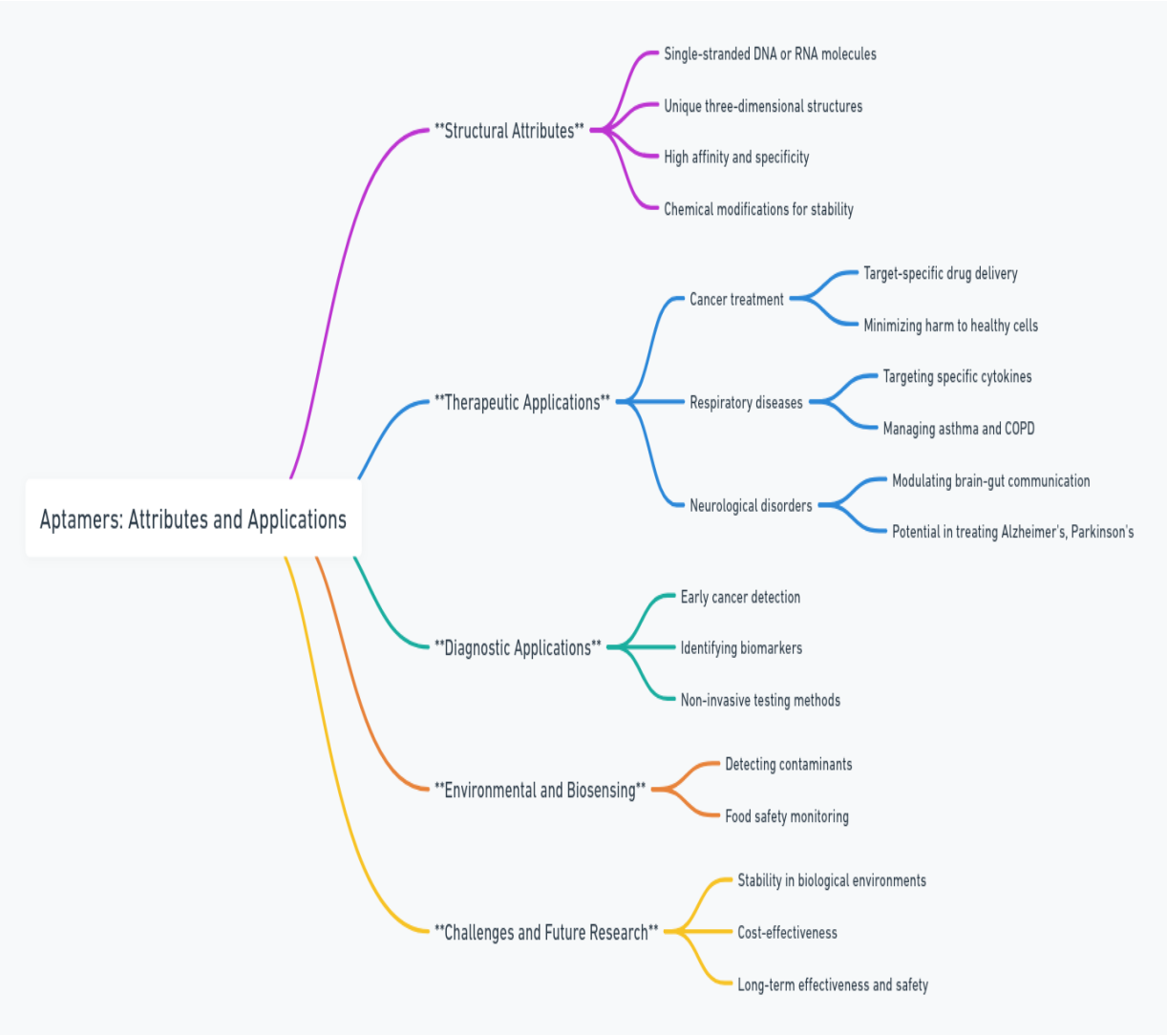

Figure 1 Aptamers: Structural Complexity, Therapeutic Versatility, and Developmental Challenges. This schematic illustrates the structural properties of aptamers, their applications in therapy and diagnosis, and the challenges encountered in their development and clinical use.

History:

The narrative of aptamers begins in the late 20th century, during an exciting era of discovery in the field of molecular biology [18]. Aptamers, referred to as "chemical antibodies," originate from the Latin term "aptus," meaning "to fit," and the Greek term "meros," meaning "part." Their development reflects these etymological origins [19].

The concept of aptamers emerged in the laboratories of two separate research groups, led by Larry Gold and Jack Szostak, during the early 1990s [20]. These scientists embarked on parallel paths to develop molecules that could specifically bind to target molecules, akin to antibodies, but with more versatility [21]. They employed a process known as Systematic Evolution of Ligands by Exponential Enrichment (SELEX), which facilitated the selection of short, single-stranded DNA or RNA molecules with high affinity for specific target molecules [22].

In 1990, Andrew Ellington and Jack Szostak first demonstrated the in vitro selection of RNA ligands, coining the term "aptamers". Concurrently, Larry Gold and Craig Tuerk demonstrated SELEX with RNA binding to bacteriophage T4 DNA polymerase [23]. The advent of the SELEX process marked a pivotal milestone, enabling the creation of aptamers targeting diverse entities.

The period following SELEX witnessed a transition towards enhancing the stability and functionality of aptamers through optimization. During this time, chemically modified aptamers emerged, increasing resistance to nuclease degradation and improving binding affinities [24].

Therapeutic aptamers emerged in the early 21st century. The FDA approved Macugen (pegaptanib) in 2004 as the first aptamer-based drug for treating neovascular age-related macular degeneration (AMD). This significant milestone confirmed the therapeutic capabilities of aptamers and spurred further research and development efforts.

Aptamers have become valuable tools in various domains, including therapeutics, diagnostics, and environmental sensing. The development and utilization of aptamers have undergone significant progress, leading to their widespread application in precision medicine and laying a solid groundwork for future innovations.

Structural and Functional Characterization of Aptamers

Aptamers are a crucial and adaptable component of contemporary molecular medicine. Known as "chemical antibodies," these short single-stranded DNA or RNA molecules possess remarkable recognition and binding capabilities, displaying high affinity and specificity towards diverse target molecules [25], ranging from small organic compounds and metal ions to large proteins and entire cells. Unlike antibodies, which rely on their distinctive three-dimensional structures for binding, aptamers exhibit unparalleled versatility due to their ability to fold into precise shapes that match their targets [26]. This flexibility allows them to adapt their structure precisely to specific targets, thereby demonstrating strong binding capabilities.

Aptamers have significantly transformed the field of molecular recognition and interaction, serving as valuable tools in biomedical applications. The chemical synthesis of these compounds ensures consistent quality and performance. Additionally, their thermal stability and non-immunogenic nature facilitate convenient modification or labeling without compromising their binding capabilities [27]. Aptamers possess the unique ability to bind targets that are difficult for antibodies to recognize, either due to their toxicity or lack of immunogenic properties.

Advances in Aptamer Selection

The SELEX process (Systematic Evolution of Ligands by Exponential Enrichment) is a highly effective method for identifying and optimizing aptamers, demonstrating exceptional specificity. The process begins with a large reservoir containing a diverse range of oligonucleotide sequences, estimated to be up to 10^15 in number [28].

The target molecule selectively allows the survival of molecules that can bind to it effectively, mimicking natural selection. This selection is facilitated through the partitioning and amplification of higher affinity oligonucleotides via PCR in successive rounds of selection. SELEX is versatile, functioning effectively in both physiological and harsh environments [29], and is highly valuable for applications in diagnostics and therapeutics.

Moreover, the integration of Next-Generation Sequencing (NGS) with SELEX techniques has had a transformative impact. This integration has not only facilitated the consolidation of millions of DNA sequences but has also enhanced scientists' ability to identify rare yet highly specific aptamers with improved precision and efficiency [30]. NGS with SELEX provides researchers opportunities to investigate sequence diversity and enhance the selection process from existing aptamer libraries.

Advancements and Challenges in Enhancing Aptamer Stability and Specificity

Aptamers possess several advantages, yet their stability and specificity require enhancement for increased practicality. Scientists have addressed the issue of nucleases degrading aptamers in biological environments by implementing innovative approaches. These include incorporating chemical modifications such as 2'-fluoro, 2'-amino, and 2'-O-methyl substitutions into the aptamer's sequence structure. Additionally, protective carriers like nanoparticles and liposomes have been utilized to enhance resistance against nucleases [31]. Advances in specificity have been achieved through refined Systematic Evolution of Ligands by Exponential Enrichment (SELEX) protocols and advanced bioinformatics tools. These developments have enabled a more precise selection process for non-targets and a deeper understanding of the interaction between aptamers and targets.

Aptamers and Gastrointestinal Health

As research on the gastrointestinal (GI) tract's impact on health and disease expands, the therapeutic and diagnostic applications of aptamers also show promise. The complex nature of this system makes it vulnerable to various diseases, such as inflammatory bowel diseases and gastric cancers, providing a favorable opportunity for aptamer intervention. Aptamers have demonstrated diagnostic potential for colorectal cancer, a prevalent and highly dangerous gastrointestinal malignancy. They achieve this by identifying and binding to proteins or other molecular markers that are abnormally expressed in the presence of the disease, enabling early detection and facilitating prompt implementation of preventive or minimization treatments.

Aptamers have been identified as a promising tool for targeted treatments in the fight against gastrointestinal (GI) diseases, as indicated in Table 1. They can be engineered to specifically target and inhibit pro-inflammatory cytokines, which play a central role in the development of inflammatory bowel disease (IBD) [32]. This strategy offers an advanced approach with fewer side effects compared to current therapies. Additionally, there is promise in using aptamers to manipulate gut microbiota for therapeutic benefit [33-35], a concept gaining recognition due to its significant role in health and disease.

Aptamers and Oral Health

The oral cavity is a multifaceted ecosystem, hosting a wide array of microorganisms and tissues. It also serves as a pathway to oral diseases, such as periodontal disease and cancer, which can significantly impact overall health and well-being. Aptamers have revolutionized oral healthcare by enabling advancements in diagnostics and treatment monitoring. Salivary aptamers are currently under investigation for their potential application in noninvasive early detection of various conditions, including cancer, a prevalent form of malignancy globally [53, 54]. This method may enable cost-effective saliva tests for early detection of cancer biomarkers, leading to improved treatment outcomes for patients.

Table 1 This table presents a summary of various gastrointestinal conditions, the aptamers used to treat them, their mechanisms of action, and the corresponding scientific references. Each entry describes a specific aptamer's function in disease management, as reported in the literature cited.

Gastrointestinal Condition	Aptamer Types	Mechanism of Action	References
Inflammatory Bowel Disease (IBD)	TNF-α aptamer	Binds to and neutralizes TNF-α, reducing inflammation	[32]
Celiac Disease	Gliadin aptamer	Binds to gliadin, blocking its interaction with the intestinal epithelium	[36]
Gastritis	Leukotriene B4 aptamer	Binds to and inhibits leukotriene B4, reducing inflammation	[37]
Helicobacter pylori Infection	Urease aptamer	Binds to urease enzyme, inhibiting H. pylori colonization	[38]
Hemorrhoids	VEGF aptamer	Inhibits VEGF, reducing hemorrhoidal bleeding	[39]
Crohn's Disease	IL-6 aptamer	Binds to IL-6, reducing inflammation and disease activity	[40]
Irritable Bowel Syndrome (IBS)	5-HT4 aptamer	Binds to 5-HT4 receptors, modulating gut motility	[41]
Diverticulitis	TNF-α aptamer	Binds to and neutralizes TNF-α, reducing inflammation	[42]
Constipation	L-type Calcium Channel aptamer	Modulates L-type Calcium Channel, improving gut motility	[43]
Hepatic Cirrhosis	TGF-β1 aptamer	Binds to and inhibits TGF-β1, preventing liver fibrosis	[44]
Non-alcoholic Fatty Liver Disease (NAFLD)	FABP4 aptamer	Binds to FABP4, reducing lipid accumulation in the liver	[45]
Gastrointestinal Bleeding	Thrombin aptamer	Binds to and inhibits thrombin, preventing blood clot formation	[46]
Gastroenteritis	Aptamer against bacterial toxins	Neutralizes bacterial toxins, preventing damage to the gut lining	[47]
Gastroesophageal Reflux Disease (GERD)	PPI-aptamer	Inhibits proton pump action, reducing stomach acid production	[48]
Ulcerative Colitis	NF-κB aptamer	Inhibits NF-κB, reducing inflammation and promoting mucosal healing	[49]
Pancreatitis	Trypsin aptamer	Inhibits trypsin, reducing inflammation and pancreatic damage	[50]
Gallstones	Cholesterol aptamer	Binds to cholesterol in bile, preventing gallstone formation	[51]
Fatty Liver Disease	SREBP-1c aptamer	Inhibits SREBP-1c, reducing lipid accumulation in the liver	[52]

Abbreviations: TNF: tumor necrosis factor, VEGF: vascular endothelial growth factor, IL: Interleukin, 5-HT: 5-hydroxytryptamine, TGF: Transforming Growth Factor, FABP4: fatty acid-binding protein 4, PPI: Proton Pump Inhibitors, NF-κB: Nuclear Factor kappa-light-chain-enhancer of activated B cells, SREBP: Sterol Regulatory Element-Binding Protein.

Aptamers provide a novel approach for treating oral diseases, as indicated in Table 2. Periodontal disease, characterized by chronic inflammation and tissue damage, can be effectively addressed by utilizing aptamers. These molecules have the ability to specifically target crucial inflammatory mediators or pathogenic bacteria, thereby impeding the advancement of the disease [55]. Furthermore, aptamers have shown significant promise in addressing oral cancer. Specifically, aptamers engineered to bind and inhibit oncogenic proteins within cancer cells selectively have yielded remarkable outcomes in preclinical investigations.

Moreover, the incorporation of aptamers into dental materials has the potential to significantly enhance restorative dentistry. These aptamers can be integrated into materials to confer antimicrobial capabilities or promote tissue regeneration.

Table 2 This table provides a concise overview of various oral conditions, the aptamers used for their management, their mechanisms of action, and the associated references. Each row specifies an aptamer's role in influencing a particular oral condition, as supported by the referenced studies.

Oral Condition	Aptamer	Mechanism of Action	References
Oral Leukoplakia	EpCAM Aptamer	Reduces cell proliferation, potentially halting disease progression	[56]
Halitosis (Bad Breath)	H2S Aptamer	Detects and quantifies halitosis related H2S	[57]
Oral Mucositis	TLR4 Aptamer	Blocks TLR4, reducing inflammation and ulceration	[58]
Oral Candidiasis	Candida Aptamer	Binds to Candida species, preventing biofilm formation	[59]
Oral Lichen Planus	EpCAM Aptamer	Targeting EpCAM positive cells, reducing proliferation	[60]
Oral Ulcers	VEGF165 Aptamer	Inhibits angiogenesis, promoting wound healing	[61]
Gingivitis	TNF-α Aptamer	Blocks TNF-α, reducing inflammation	[62]
Dental Caries	S. Mutans Aptamer	Binds to and inhibits S. Mutans, a leading cause of dental caries	[63]
Periodontitis	RANKL Aptamer	Inhibits RANKL, reducing bone loss in periodontitis	[55]
Dental Plaque	S. Mutans Aptamer	Inhibits S. Mutans, a leading cause of dental plaque	[64]

Abbreviations: EpCAM: Epithelial Cell Adhesion Molecule, H2S: Hydrogen Sulfide, TLR: Toll-Like Receptor, VEGF: vascular endothelial growth factor, TNF: tumor necrosis factor, RANKL: Receptor Activator of Nuclear Factor Kappa-B Ligand

Aptamer-Based Targeted Therapy in Oncology

Aptamers in oncology have the potential to revolutionize cancer treatment through targeted therapy [65]. This is exemplified by their successful application in various types of cancer, as shown in Table 3. The AS1411 aptamer exhibits notable versatility by effectively targeting both colorectal and ovarian cancers [66, 67], showcasing the broad applicability of aptamers. AS1411 inhibits cell proliferation by binding to nucleolin, a protein that is overexpressed in numerous cancer cells. This targeted approach minimizes potential harm to healthy tissues, making it highly valuable in the treatment of aggressive cancers such as colorectal cancer [66], where minimizing collateral damage is crucial. It is also beneficial in the case of ovarian cancer, where early detection is challenging, and precise treatments are essential.

The MUC1 aptamer specifically binds to the MUC1

antigen, which is highly expressed in gastric and pancreatic cancers. The specificity of the aptamer allows for targeted interference with tumor cell growth and metastasis. The focused application of the MUC1 aptamer holds great promise in the context of pancreatic cancer [68], a disease known for its resistance to standard therapies and aggressive progression. The MUC1 aptamer has the potential to improve cancer treatment by selectively targeting cancer cells [68], potentially leading to more effective therapies with fewer side effects, which is a significant development in managing these complex malignancies.

The A10 PSMA aptamer demonstrates the potential of aptamers in precision medicine for prostate cancer, a common malignancy known for its high levels of prostate-specific membrane antigen (PSMA) expression [69]. The aptamer's specific binding to PSMA allows for targeted elimination of cancer cells, presenting a promising treatment approach that may improve effectiveness and minimize the typical side effects associated with prostate cancer therapies.

These diverse applications demonstrate the versatility and precision of aptamers in targeting various cancer types. The effectiveness of aptamers such as AS1411 in treating multiple types of cancers, along with the specific targeting capabilities of aptamers like MUC1 and A10 PSMA, underscores the potential of aptamers to significantly enhance personalized cancer therapy.

Table 3 This table summarizes different cancer types, the respective aptamers used for their treatment, their mechanisms of action, and the corresponding research references. Each entry illustrates how a specific aptamer works against a particular type of cancer, as detailed in the cited research.

Cancer Type	Aptamer	Mechanism of Action	References
Colorectal Cancer	AS1411 Aptamer	Binds nucleolin and inhibits cancer cell proliferation	[66]
Gastric Cancer	MUC1 Aptamer	Targets MUC1 on cancer cells and inhibits proliferation	[68]
Prostate Cancer	A10 PSMA Aptamer	Binds to PSMA, selectively targeting and killing prostate cancer cells	[69]
Ovarian Cancer	AS1411 Aptamer	Binds nucleolin, inhibiting cancer cell proliferation	[67]
Skin Cancer	VEGF Aptamer	Inhibits angiogenesis, hindering tumor growth	[70]
Breast Cancer	Her2 Aptamer	Targets Her2, selectively killing breast cancer cells	[71]
Pancreatic Cancer	MUC1 Aptamer	Binds to MUC1 on pancreatic cancer cells, inhibiting proliferation	[72]
Cervical Cancer	EpCAM Aptamer	Binds to EpCAM on cancer cells, inhibiting proliferation	[73]
Bladder Cancer	EpCAM Aptamer	Targets EpCAM on bladder cancer cells, inhibiting proliferation	[74]
Lung Cancer	AXL Aptamer	Targets AXL receptor, inducing apoptosis in cancer cells	[75]
Liver Cancer	ASGPR Aptamer	Targets ASGPR on liver cancer cells, inhibiting proliferation	[76]

Abbreviations: MUC: Mucin, PSMA: Prostate-Specific Membrane Antigen, VEGF: vascular endothelial growth factor, HER: Human Epidermal Growth Factor Receptor, EpCAM: Epithelial Cell Adhesion Molecule, ASGPR: Asialoglycoprotein Receptor.

Aptamers and Airway Inflammation

Managing the inflammatory nature of respiratory diseases such as asthma and COPD poses significant challenges. Aptamers offer an ideal solution as they minimize side effects associated with conventional treatments, which lack specificity. Aptamers are single-stranded DNA or RNA molecules that possess a distinct ability to recognize and bind to specific targets due to their unique three-dimensional structure [20]. This enables them to bind strongly yet specifically to proteins, small molecules, and even cells without inducing any immune response while simultaneously avoiding off-target effects

due to their size [77].

Tralokinumab, an aptamer designed to target interleukin-13 (IL-13), has demonstrated remarkable potential in clinical trials. It has exhibited substantial efficacy in enhancing lung function and managing symptoms among individuals with asthma [78]. Similarly, TNF alpha, another key player in COPD pathogenesis, is being investigated using aptamers, and preclinical models show promising results as well [79].

Aptamers show significant potential in modulating inflammation related to respiratory diseases like asthma and COPD, offering promising opportunities to enhance existing therapeutic approaches. Aptamers are increasingly recognized as valuable diagnostic tools, offering an efficient and non-invasive approach to detect respiratory illness-associated biomarkers [80, 81].

Emerging Applications of Aptamers in Neurological Disorders

The utilization of aptamers in the field of neurological disorders signifies a notable advancement, providing accurate and focused interventions for a range of conditions as shown in Table 4. The X-Aptamer's application in schizophrenia diagnosis represents a significant breakthrough, identifying C4A and ApoB as promising biomarkers [82]. This development marks a new era in the diagnostic approach to this complex mental disorder [83], offering insights into underlying pathophysiological mechanisms and facilitating early detection and targeted therapeutic strategies.

The β-casomorphin-7 aptamer plays a crucial role in detecting β-casomorphin, representing a significant advancement in diagnostic approaches for autism spectrum disorder (ASD) [84]. This biomarker-based technique offers a more objective and potentially earlier identification of ASD, surpassing traditional behavioral assessments and enabling timely, personalized interventions.

The therapeutic use of the VEGF aptamer in spinal cord injuries demonstrates a novel approach to enhancing recovery [85]. By promoting angiogenesis, this treatment addresses a critical aspect of healing spinal cord injuries, potentially accelerating tissue regeneration and improving functional outcomes in a condition historically challenging to treat.

The RB006 aptamer's specific binding to Factor IXa in ischemic stroke management provides a precise method for regulating clot formation [86], reducing the risk of systemic bleeding—a significant concern with broad anticoagulants. This targeted intervention may improve stroke treatment outcomes by directly addressing vascular occlusion.

The P2X7 aptamer's targeting of the P2X7 receptor in chronic pain represents a novel approach to pain management [87]. Modulating this receptor crucial in pain signaling offers a promising avenue for significantly reducing pain perception, particularly beneficial in conditions with complex pain management challenges and limited treatment options.

Aptamers also play a crucial role in neurodegenerative disorders like Alzheimer's and Parkinson's diseases. The beta-amyloid aptamer in Alzheimer's disease specifically targets and inhibits the aggregation of beta-amyloid plaques [88], potentially slowing disease progression. In Parkinson's disease, the alpha-synuclein aptamer shows promise by inhibiting alpha-synuclein aggregation [89], a departure from current symptomatic treatments toward disease-modifying approaches.

Versatile Applications of Aptamers Across Therapeutics, Diagnostics, and Environmental Monitoring

Aptamers are highly versatile and promising tools with a wide range of applications in fields such as therapeutics, diagnostics, environmental monitoring, and biosensing. Aptamers, exemplified by Pegaptanib, have significantly transformed the therapeutic approach to age-related macular degeneration by precisely targeting pathologic proteins [100, 101]. They offer high specificity and sensitivity in diagnostic tests for conditions such as cancer or infectious diseases [102].

Table 4 This table offers a brief overview of several disorders, the relevant aptamers used for their potential treatment or biomarker identification, their mechanisms of action, and the associated scientific references. Each row specifies an aptamer's role in modulating or detecting a particular disorder, as supported by the referenced studies.

Disorder	Aptamer	Mechanism of Action	References
Schizophrenia	**X-Aptamer**	**Identifies C4A and ApoB in Blood as Potential Markers**	**[82]**
Autism Spectrum Disorder	β-casomorphin-7 (BCM-7) Aptamer	detection of the β-casomorphin (BCM-7) as a promising biomarker of autism disorder	**[84]**
Spinal Cord Injury	VEGF Aptamer	Binds to Vascular Endothelial Growth Factor (VEGF), promoting angiogenesis and recovery	**[85]**
Ischemic Stroke	RB006 Aptamer	Binds to Factor IXa, reducing clot formation	**[86]**
Chronic Pain	P2X7 Aptamer	Binds to P2X7 receptor, reducing pain signaling	**[87]**
Prion Diseases	PrP Aptamer	Binds to prion protein, reducing its pathological conformation	**[90]**
Multiple Sclerosis	MBP-1 Aptamer	Binds to myelin basic protein, modulating immune response	**[91]**
Huntington's Disease	guanine-rich aptamers	showing high efficacy in modulating the functions of the mutated protein	**[92]**
Diabetic Neuropathy	NfL Aptamer	Binds to Neurofilament Light, a biomarker for nerve damage, enabling monitoring and potential therapeutic interventions	**[93]**
Fragile X Syndrome	FMRP Aptamer	Binds to Fragile X Mental Retardation Protein, potential therapeutic applications for genetic disorders	[94]
Myasthenia Gravis	Acetylcholine Receptor Aptamer	Binds to Acetylcholine Receptor, potentially reducing autoantibody-mediated damage	[95]
Dementia	BACE1 Aptamer	Inhibits BACE1 enzyme, reducing amyloid-beta production	**[96]**
Alzheimer's Disease	beta-amyloid Aptamer	Binds to beta-amyloid, inhibiting its aggregation	**[88]**
Parkinson's Disease	alpha-synuclein Aptamer	Binds to alpha-synuclein, inhibiting its aggregation	**[89]**
Amyotrophic Lateral Sclerosis (ALS)	SOD1 Aptamer	Binds to superoxide dismutase 1 (SOD1), reducing its aggregation	**[97]**
Stroke/Ischemia	NMDA receptor Aptamer	Binds to NMDA receptors, reducing glutamate-induced neurotoxicity	**[98]**
Tourette Syndrome	Dopamine D2 Receptor Aptamer	Binds to Dopamine D2 Receptor, potential for use in adjusting dopaminergic signaling	[99]

Abbreviations: C4A: Complement Component 4A, Apo: Apolipoprotein, PrP: Prion Protein, MBP: Myelin Basic Protein, NfL: Neurofilament Light, FMRP: Fragile X Mental Retardation Protein, BACE: Beta-Site APP Cleaving Enzyme, SOD: Superoxide Dismutase, NMDA: N-Methyl-D-Aspartate.

In environmental protection, aptamers play a significant role by cost-effectively detecting contaminants like mercury, ensuring food safety through the identification of foodborne pathogens [103]. Furthermore, they serve as carriers for transporting therapeutic agents to specific cells, thereby reducing overall toxicity in cancer therapy [104].

Limitations and Delivery Methods of Aptamers in Therapeutic Applications

Aptamers, despite being recognized for their specificity and potential in targeted therapies, encounter several fundamental limitations that hinder their clinical applicability. One major consideration is the stability of these entities in the biological environment [105]. Aptamers, especially those based on RNA, are susceptible to degradation by nucleases in the body's fluids [106], leading to a notable reduction in their therapeutic effectiveness. To address this problem, significant efforts have been focused on chemical modifications, including the integration of unnatural nucleotide analogs, which can provide resistance against nucleases [107]. Nevertheless, these modifications may unintentionally impact the aptamer's binding affinity or specificity, as well as increase production costs, which could hinder the feasibility of large-scale manufacturing and widespread clinical implementation. The specificity of aptamers poses challenges despite being a defining characteristic. In the complex and diverse environment of the human body, it is important to consider the potential for aptamers to bind to molecules that are not their intended targets or to similar regions on different cells. The lack of specificity in binding raises concerns regarding potential off-target effects [108], which may result in unfavorable outcomes. It is crucial to carefully optimize the structure of the aptamer and conduct thorough in vivo testing in order to minimize these risks. Aptamers are commonly considered to have lower immunogenicity compared to protein-based therapeutics with respect to their immunogenic properties [109]. Nonetheless, the immune response may still occur to some extent, particularly when the administration is repeated or prolonged. Minimizing immunogenic responses is crucial in the development of aptamers, especially for long-term therapeutic use. In the field of delivery methods, various innovative strategies have been developed to improve the effectiveness of aptamer therapeutics. Nanoparticle-based delivery systems have become increasingly important due to their ability to protect aptamers from enzymatic degradation [110] and facilitate targeted and controlled release. Nanoparticles can be customized to target specific cell types or tissues, thereby improving the therapeutic effectiveness of aptamers. Conjugation techniques involve attaching aptamers to different carriers such as lipids, polymers, or other biological molecules [111]. This strategy aims to enhance the bioavailability and prolong the half-life of aptamers. Conjugates can enhance tissue penetration, particularly in dense or inaccessible regions, and assist in targeting specific cellular sites for aptamer delivery. Local administration of aptamers, particularly in diseases such as cancer, provides a means to enhance therapeutic efficacy at the specific target site while minimizing systemic exposure [112]. This approach is particularly applicable to solid tumors, as localized treatment can greatly enhance effectiveness. Exosome-based systems offer a promising approach for delivering aptamers [113, 114], representing a new and innovative method in the field of delivery methods. Exosomes, being natural carriers, can encapsulate aptamers, thereby protecting them from degradation and facilitating precise delivery to particular cell types. Hydrogel-based delivery systems are gaining attention in regenerative medicine due to their capacity for localized and sustained release of aptamers [115].

CONCLUSION

Aptamers, single-stranded nucleic acids, show immense promise in diagnosing and treating a variety of diseases, including oncology, respiratory conditions like asthma and chronic obstructive pulmonary disease (COPD), and neurological disorders. These compounds

demonstrate high specificity and affinity towards diverse targets, enabling precise interventions with reduced toxicity. Aptamers hold potential for early cancer detection and immunotherapy. In respiratory diseases, targeting specific cytokines offers therapeutic advantages over conventional treatments.

Preliminary research suggests aptamers may also influence neurological disorders by modulating gut-brain communication. However, challenges remain in ensuring their stability, kinetics in living organisms, and cost-effectiveness. Further research is essential to optimize these parameters and validate the long-term effectiveness and safety of aptamers. Despite these challenges, aptamers possess significant versatility and potential to profoundly impact healthcare, warranting continued investigation.

REFERENCES

1. Liu S., Xu Y., Jiang X., Tan H., Ying B. Translation of aptamers toward clinical diagnosis and commercialization. *Biosensors and Bioelectronics.* 2022; 208: 114168.
2. Sasso J.M., Ambrose B.J., Tenchov R., Datta R.S., Basel M.T., DeLong R.K., Zhou Q.A. The Progress and promise of RNA medicine─ An arsenal of targeted treatments. *J Med Chem.* 2022; 65 (10): 6975-7015.
3. Pranay K., Gupta M.K., Devi S., Sharma N., Anand A. Challenges of aptamers as targeting ligands for anticancer therapies. *Aptamers Engineered Nanocarriers for Cancer Therapy: Elsevier.* 2023; 455-480.
4. Das S., Gupta A., Vaishnavi T., Walia S., Bhatia D., Chakraborty B. Aptamers functionalized biomolecular nano-vehicles for applications in cancer diagnostics & therapeutics. *Applied NanoMedicine.* 2022; 2 (2): 360-360.
5. Schanzenbacher J., Kähler K.H., Mesler E., Kleingarn M., Karsten C.M., Seiler D.L. The role of C5a receptors in autoimmunity. *Immunobiology.* 2023: 152413.
6. Raffaele I., Silvestro S., Mazzon E. MicroRNAs and MAPKs: Evidence of These Molecular Interactions in Alzheimer's Disease. *Int J Mol Sci.* 2023; 24 (5): 4736.
7. Accortt E., Mirocha J., Zhang D., Kilpatrick S.J., Libermann T., Karumanchi S.A. Perinatal mood and anxiety disorders: biomarker discovery using plasma proteomics. *Am J Obstet Gynecol.* 2023.
8. Ahmad A. Precision Medicine and Pharmacogenetics: Stratification and Improved Outcome in Non-Small Cell Lung Cancer. *Jordan Journal of Pharmaceutical Sciences.* 2023; 16 (2): 441-441.
9. Hakooz N. Pharmacogenetics and Personalized Medicines. *Jordan Journal of Pharmaceutical Sciences.* 2023; 16 (2): 444-444.
10. Bahti A., Telfah A., Sharar N., Jafar H., Hergenröder R. Nuclear Magnetic Resonance for Targeted Metabolomics and Biochemical Sensor. *Jordan Journal of Pharmaceutical Sciences.* 2023; 16(2):469-469.
11. Siwak A.M. Nanostructured immunosensor for low level detection of waterborne cryptosporidium. 2022.
12. Stephens M., Keane K., Roizes S., Liao S., Von der Weid P-Y. Mincle-binding DNA aptamer demonstrates therapeutic potential in a model of inflammatory bowel disease. *Molecular Therapy-Nucleic Acids.* 2022; 28:935-947.
13. Vargas E., Nandhakumar P., Ding S., Saha T., Wang J. Insulin detection in diabetes mellitus: challenges and new prospects. *Nature Reviews Endocrinology.* 2023:1-9.
14. Omidian H., Mfoafo K. Exploring the Potential of Nanotechnology in Pediatric Healthcare: Advances, Challenges, and Future Directions. *Pharmaceutics.* 2023; 15(6):1583.

15. Stephens M. The emerging potential of Aptamers as therapeutic agents in infection and inflammation. *Pharmacol Ther.* 2022; 238:108173.
16. Li W., Wang C., Wang Z., Gou L., Zhou Y., Peng G. et al. Physically cross-linked DNA hydrogel-based sustained cytokine delivery for in situ diabetic alveolar bone rebuilding. *ACS Applied Materials & Interfaces.* 2022; 14(22):25173-25182.
17. Burchett J.R., Dailey J.M., Kee S.A., Pryor D.T., Kotha A., Kankaria R.A. et al. Targeting mast cells in allergic disease: current therapies and drug repurposing. *Cells.* 2022; 11(19):3031.
18. Shraim AaS., Abdel Majeed BA., Al-Binni MA., Hunaiti A. Therapeutic Potential of Aptamer–Protein Interactions. *ACS Pharmacology & Translational Science.* 2022; 5(12):1211-1227.
19. Nava G., Zanchetta G., Giavazzi F., Buscaglia M. Label-free optical biosensors in the pandemic era. *Nanophotonics.* 2022; 11(18):4159-4181.
20. Kenguva G., Rout SR., Giri L., Sahebkar A., Kesharwani P., Dandela R. Cell-SELEX technology for aptamer selection. *Aptamers Engineered Nanocarriers for Cancer Therapy: Elsevier.* 2023; 1-20.
21. Ortega G., Chamorro-Garcia A., Ricci F., Plaxco KW. On the rational design of cooperative receptors. *Annual Review of Biophysics.* 2023; 52:319-337.
22. Chen Z., Luo H., Gubu A., Yu S., Zhang H., Dai H. et al. Chemically modified aptamers for improving binding affinity to the target proteins via enhanced non-covalent bonding. *Frontiers in Cell and Developmental Biology.* 2023; 11:1091809.
23. Razlansari M., Jafarinejad S., Rahdar A., Shirvaliloo M., Arshad R., Fathi-Karkan S. et al. Development and classification of RNA aptamers for therapeutic purposes: An updated review with emphasis on cancer. *Molecular and Cellular Biochemistry.* 2022:1-26.
24. Qi S., Duan N., Khan IM., Dong X., Zhang Y., Wu S., Wang Z. Strategies to manipulate the performance of aptamers in SELEX, post-SELEX and microenvironment. *Biotechnol Adv.* 2022; 55:107902.
25. Jaisankar A., Krishnan S., Rangasamy L. Recent developments of aptamer-based lateral flow assays for point-of-care (POC) diagnostics. *Anal Biochem.* 2022: 114874.
26. Tiwari R., Gulbake A., Kumar P., Gulbake AS., Gupta R., Bisht D., Sethiya NK. Aptamer-Based Targeted Drug Delivery Systems. *Pharmaceutical Nanobiotechnology for Targeted Therapy: Springer.* 2022; 93-122.
27. Gan Z., Roslan MAM., Abd Shukor MY., Halim M., Yasid NA., Abdullah J. et al. Advances in Aptamer-Based Biosensors and Cell-Internalizing SELEX Technology for Diagnostic and Therapeutic Application. *Biosensors.* 2022; 12(11):922.
28. Lim M-C., Lim ES., Lim J-A., Choi S-W., Chang H-J. Efficient Screening of Pesticide Diazinon-Binding Aptamers Using the Sol–Gel-Coated Nanoporous Membrane-Assisted SELEX Process and Next-Generation Sequencing. *Applied Biochemistry and Biotechnology.* 2022; 194(9):3901-3913.
29. Halloy F., Biscans A., Bujold KE., Debacker A., Hill AC., Lacroix A. et al. Innovative developments and emerging technologies in RNA therapeutics. *RNA Biol.* 2022; 19(1):313-332.
30. Mashayekhi K., Ganji A., Sankian M. Designing a new dimerized anti human TNF-α aptamer with blocking activity. *Biotechnology Progress.* 2020; 36(4):e2969.
31. Castro J., Barros MM., Araújo D., Campos AM., Oliveira R., Silva S., Almeida C. Swine enteric colibacillosis: Current treatment avenues and future directions. *Frontiers in Veterinary Science.* 2022; 9:981207.

32. Xing H., Zhang Y., Krämer M., Kissmann A-K., Amann V., Raber HF. et al. A polyclonal Aptamer library for the specific binding of the gut bacterium Roseburia intestinalis in mixtures with other gut microbiome Bacteria and human stool samples. *Int J Mol Sci.* 2022; 23(14):7744.
33. Doherty MK., Shaw C., Woods L., Weimer BC. Alpha-Gal Bound Aptamer and Vancomycin Synergistically Reduce Staphylococcus aureus Infection In Vivo. *Microorganisms.* 2023; 11(7):1776.
34. Bhakta S., Mishra P. Molecularly imprinted polymer-based sensors for cancer biomarker detection. *Sensors and Actuators Reports.* 2021; 3:100061.
35. Zhang Z., Kurashima Y. Two sides of the coin: Mast cells as a key regulator of allergy and acute/chronic inflammation. *Cells.* 2021; 10(7): 1615.
36. Wu J., Zhu X., Guo X., Yang Z., Cai Q., Gu D. et al. Helicobacter urease suppresses cytotoxic CD8+ T-cell responses through activating Myh9-dependent induction of PD-L1. *Int Immunol.* 2021; 33(9):491-504.
37. Siddique R., Khan S., Bai Q., Li H., Ullah MW., Xue M. Arsenic Trioxide-based nanomedicines as a therapeutic combination approach for treating gliomas: a review. *Current Nanoscience.* 2021; 17(3): 406-417.
38. Ando T., Yamamoto M., Takamori Y., Tsukamoto K., Fuji D., Kawakami T. In vitro selection of an RNA aptamer yields an interleukin-6/interleukin-6 receptor interaction inhibitor. *Bioscience, Biotechnology, and Biochemistry.* 2021; 85(5):1170-1174.
39. Zogg H. miR-10b Rescues Diabetes and GI Dysmotility Associated with a Leaky Gut. *University of Nevada, Reno.* 2022.
40. Hu X-M., Li Z-X., Zhang D-Y., Yang Y-C., Zheng S-Y., Zhang Q. et al. Current research and clinical trends in rosacea pathogenesis. *Heliyon.* 2022.
41. Mazumder K., Aktar A., Roy P., Biswas B., Hossain ME., Sarkar KK. et al. A review on mechanistic insight of plant derived anticancer bioactive Phytocompounds and their structure activity relationship. *Molecules.* 2022; 27(9):3036.
42. Wang L., Feng J., Deng Y., Yang Q., Wei Q., Ye D. et al. Ccaat/enhancer-binding proteins in fibrosis: complex roles beyond conventional understanding. *Research.* 2022; 2022.
43. Bayarsaikhan G., Bayarsaikhan D., Lee J., Lee B. Targeting scavenger receptors in inflammatory disorders and oxidative stress. *Antioxidants.* 2022; 11(5):936.
44. Reed CR., Bonadonna D., Otto JC., McDaniel CG., Chabata CV., Kuchibhatla M. et al. Aptamer-based factor IXa inhibition preserves hemostasis and prevents thrombosis in a piglet model of ECMO. *Molecular Therapy-Nucleic Acids.* 2022; 27:524-534.
45. Pierzynowska K., Morcinek-Orłowska J., Gaffke L., Jaroszewicz W., Skowron PM., Węgrzyn G. Applications of the phage display technology in molecular biology, biotechnology and medicine. *Crit Rev Microbiol.* 2023:1-41.
46. Foret F., Chung DS., Lavická J., Přikryl J., Lee H., Drobníková I. Proceedings of APCE-CECE-ITP-IUPAC 2022. *MDPI.* 2023.
47. Li X., Mo K., Tian G., Zhou J., Gong J., Li L., Huang X. Shikimic Acid Regulates the NF-κB/MAPK Signaling Pathway and Gut Microbiota to Ameliorate DSS-Induced Ulcerative Colitis. *J Agric Food Chem.* 2023.
48. Yu J., Boland L., Catt M., Puk L., Wong N., Krockenberger M. et al. Serum proteome profiles in cats with chronic enteropathies. *J Vet Intern Med.* 2023.
49. Belkadi A., Thareja G., Abbaszadeh F., Badii R., Fauman E., Albagha OM., Suhre K. Identification of PCSK9-like human gene knockouts using metabolomics, proteomics, and whole-genome sequencing in a consanguineous population. *Cell Genomics.* 2023; 3(1).

50. Xu S-M., Xu Y., Cheng X-G., Yang L-Q. Tilianin Protects against Nonalcoholic Fatty Liver Disease in Early Obesity Mice. *Biol Pharm Bull.* 2023; 46(3): 419-426.
51. Papale F., Santonocito S., Polizzi A., Giudice AL., Capodiferro S., Favia G., Isola G. The new era of salivaomics in dentistry: frontiers and facts in the early diagnosis and prevention of oral diseases and cancer. *Metabolites.* 2022; 12(7): 638.
52. Buchan E., Hardy M., Gomes PdC., Kelleher L., Chu HOM., Oppenheimer PG. Emerging Raman spectroscopy and saliva-based diagnostics: from challenges to applications. *Appl Spectrosc Rev.* 2022:1-38.
53. Rouco Taboada H., García García P., Briffault del Castillo EB., Díaz Rodríguez P. Modulating osteoclasts with nanoparticles: A path for osteoporosis management? 2023.
54. Yáñez-Sedeño P., Campuzano S., Pingarrón J. Pushing the limits of electrochemistry toward challenging applications in clinical diagnosis, prognosis, and therapeutic action. *Chem Commun.* 2019; 55(18):2563-2592.
55. Rahm CE. Carbon nanotube sensor design and fabrication for determining lead in drinking water and ammonia gas in the air. *University of Cincinnati.* 2022.
56. Büyükköroğlu G., Şenel B., Şalva E., Çalışkan B. Biotechnology applications in clinical trials. In: Biotechnology in Healthcare: Elsevier 2022; 163-195.
57. Kneißle K., Krämer M., Kissmann A-K., Xing H., Müller F., Amann V. et al. A Polyclonal SELEX Aptamer Library Allows Differentiation of Candida albicans, C. auris and C. parapsilosis Cells from Human Dermal Fibroblasts. *J Fungi.* 2022; 8(8):856.
58. Shi S., Yu Z-L., Jia J. The Roles of Exosomes in the Diagnose, Development and Therapeutic Resistance of Oral Squamous Cell Carcinoma. *Int J Mol Sci.* 2023; 24(3):1968.
59. Lyu S., Dong Z., Xu X., Bei H-P., Yuen H-Y., Cheung C-WJ. et al. Going below and beyond the surface: Microneedle structure, materials, drugs, fabrication, and applications for wound healing and tissue regeneration. *Bioactive Materials.* 2023; 27:303-326.
60. Irimeș MB., Tertiș M., Oprean R., Cristea C. Unrevealing the connection between real sample analysis and analytical method. The case of cytokines. *Med Res Rev.* 2023.
61. Ming J., Zeng X., Zhou R. Portable biosensor-based oral pathogenic bacteria detection for community and family applications. *Anal Bioanal Chem.* 2023:1-13.
62. Mohammed RK., Ibrahim AA. The anti-adherence activity and bactericidal effect of GO against Streptococcus mutans from Iraqi dental patients. *Odontology.* 2023:1-7.
63. Yang C., Jiang Y., Hao SH., Yan XY., Naranmandura H. Aptamers: an emerging navigation tool of therapeutic agents for targeted cancer therapy. *J Mater Chem B.* 2022; 10(1):20-33.
64. Hosseini NF., Amini R., Ramezani M., Saidijam M., Hashemi SM., Najafi R. AS1411 aptamer-functionalized exosomes in the targeted delivery of doxorubicin in fighting colorectal cancer. *Biomed Pharmacother.* 2022; 155:113690.
65. Zhao J., Tan W., Zheng J., Su Y., Cui M. Aptamer nanomaterials for ovarian cancer target theranostics. *Front Bioeng Biotechnol.* 2022; 10:884405.
66. Qing L., Li Q., Dong Z. MUC1: An emerging target in cancer treatment and diagnosis. *Bull Cancer.* 2022.
67. Cruz-Hernández CD., Rodríguez-Martínez G., Cortés-Ramírez SA., Morales-Pacheco M., Cruz-Burgos M., Losada-García A. et al. Aptamers as theragnostic tools in prostate cancer. *Biomolecules.* 2022; 12(8):1056.
68. Zhou Y., Yu Y., Lv H., Zhang H., Liang T., Zhou G. et al. Apigenin in cancer therapy: From mechanism of action to nano-therapeutic agent. *Food Chem Toxicol.* 2022; 113385.

69. Sheikh A., Md S., Kesharwani P. Aptamer grafted nanoparticle as targeted therapeutic tool for the treatment of breast cancer. *Biomed Pharmacother.* 2022; 146:112530.
70. Li W., Han Y., Sun C., Li X., Zheng J., Che J. et al. Novel insights into the roles and therapeutic implications of MUC1 oncoprotein via regulating proteins and non-coding RNAs in cancer. *Theranostics.* 2022; 12(3):999.
71. Liu X., Zhang N., Chen Q., Feng Q., Zhang Y., Wang Z. et al. SNAI2 Attenuated the Stem-like Phenotype by Reducing the Expansion of EPCAMhigh Cells in Cervical Cancer Cells. *Int J Mol Sci.* 2023; 24(2):1062.
72. Liu B., Wang J., Peng Y., Zeng H., Zhang Q., Deng M. et al. CD71/CD44 dual-aptamer-gemcitabine conjugate for tumor co-targeting treatment of bladder cancer. *Chem Eng J.* 2023; 464:142597.
73. Tang Y., Zang H., Wen Q., Fan S. AXL in cancer: a modulator of drug resistance and therapeutic target. *J Exp Clin Cancer Res.* 2023; 42(1):148.
74. Kim M., Kim S-B., Kim J., Kim K-S., Kim D-E. Co-delivery of curcumin and PTTG1 siRNA by galactose receptor-targeted liposomes for enhanced anti-tumor effects in hepatocellular carcinoma. *J Drug Deliv Sci Technol.* 2023:104692.
75. Chen Y., Tandon I., Heelan W., Wang Y., Tang W., Hu Q. Proteolysis-targeting chimera (PROTAC) delivery system: Advancing protein degraders towards clinical translation. *Chem Soc Rev.* 2022; 51(13):5330-5350.
76. Maher TM., Nambiar AM., Wells AU. The role of precision medicine in interstitial lung disease. *Eur Respir J.* 2022; 60(3).
77. Clower L., Fleshman T., Geldenhuys WJ., Santanam N. Targeting oxidative stress involved in endometriosis and its pain. *Biomolecules.* 2022; 12(8):1055.
78. Patil AA., Kaushik P., Jain RD., Dandekar PP. Assessment of Urinary Biomarkers for Infectious Diseases Using Lateral Flow Assays: A Comprehensive Overview. *ACS Infect Dis.* 2022; 9(1):9-22.
79. Chen X., Zhou S., Wang Y., Zheng L., Guan S., Wang D. et al. Nanopore single-molecule analysis of biomarkers: Providing possible clues to disease diagnosis. *TrAC, Trends Anal Chem.* 2023:117060.
80. Walss-Bass C., Lokesh GLR., Dyukova E., Gorenstein DG., Roberts DL., Velligan D., Volk DE. X-Aptamer Technology Identifies C4A and ApoB in Blood as Potential Markers for Schizophrenia. *Mol Neuropsychiatry.* 2019; 5(1):52-59. 10.1159/000492331
81. Cutshaw G., Uthaman S., Hassan N., Kothadiya S., Wen X., Bardhan R. The Emerging Role of Raman Spectroscopy as an Omics Approach for Metabolic Profiling and Biomarker Detection toward Precision Medicine. *Chem Rev.* 2023.
82. Shahdost-Fard F., Roushani M. Designing of an ultrasensitive BCM-7 aptasensor based on an SPCE modified with AuNR for promising distinguishing of autism disorder. *Talanta.* 2020; 209: 120506. 10.1016/j.talanta.2019.120506
83. Song D., Liu P., Shang K., Ma Y. Application and mechanism of anti-VEGF drugs in age-related macular degeneration. *Frontiers in bioengineering and biotechnology.* 2022; 10: 943915.
84. Chen X., Ma Y., Xie Y., Pu J. Aptamer-based applications for cardiovascular disease. *Frontiers in Bioengineering and Biotechnology.* 2022; 10: 1002285.
85. Hoshino Y., Okuno T., Saigusa D., Kano K., Yamamoto S., Shindou H. et al. Lysophosphatidic acid receptor1/3 antagonist inhibits the activation of satellite glial cells and reduces acute nociceptive responses. *The FASEB Journal.* 2022; 36(4): e22236.
86. Ugbaja S.C., Lawal M.M., Kumalo H.M. An Overview of β-Amyloid Cleaving Enzyme 1 (BACE1) in Alzheimer's Disease Therapy: Elucidating its Exosite-Binding Antibody and Allosteric Inhibitor. *Curr Med Chem.* 2022; 29(1):114-135.

87. Rock M., Zouganelis G.D., de Andrade A.F.B., Drake S.J., Alexiou A., Albrakati A. et al. Development and validation of anti-human Alpha synuclein DNA aptamer using computer modelling techniques—an in silico study. *Journal of Integrative Neuroscience.* 2022; 21(1):5.
88. Gomes M.P., de Lima E.V., Barros-Aragão F.G., Passos Y.M., Lemos F.S., Zamberlan D.C. et al. Prion protein complexed to a DNA aptamer induce behavioral and synapse dysfunction in mice. *Behav Brain Res.* 2022; 419: 113680.
89. Rahiman N., Mohammadi M., Alavizadeh S.H., Arabi L., Badiee A., Jaafari M.R. Recent advancements in nanoparticle-mediated approaches for restoration of multiple sclerosis. *Journal of Controlled Release.* 2022; 343:620-644.
90. Riccardi C., D'Aria F., Digilio F., Carillo M., Amato J., Fasano D. et al. Fighting the Huntington's Disease with a G-Quadruplex-Forming Aptamer Specifically Binding to Mutant Huntingtin Protein: Biophysical Characterization, In Vitro and In Vivo Studies. *Int J Mol Sci.* 2022; 23. 10.3390/ijms23094804
91. Majdinasab M., Marty J.L. Recent advances in electrochemical aptasensors for detection of biomarkers. *Pharmaceuticals.* 2022; 15(8):995.
92. Zhao X., Yang J., Wang X., Chen L., Zhang C., Shen Z. Inhibitory effect of aptamer-carbon dot nanomaterial-siRNA complex on the metastasis of hepatocellular carcinoma cells by interfering with FMRP. *Eur J Pharm Biopharm.* 2022; 174:47-55.
93. Graßhoff H., Fourlakis K., Comdühr S., Riemekasten G. Autoantibodies as biomarker and therapeutic target in systemic sclerosis. *Biomedicines.* 2022; 10(9):2150.
94. Wang Y., Zhu J., Jia W., Xiong H., Qiu W., Xu R., Lin Y. BACE1 Aptamer-Modified Tetrahedral Framework Nucleic Acid to Treat Alzheimer's Disease in an APP-PS1 Animal Model. *ACS Applied Materials & Interfaces.* 2022; 14(39):44228-44238.
95. Berrone E., Chiorino G., Guana F., Benedetti V., Palmitessa C., Gallo M. et al. SOMAscan Proteomics Identifies Novel Plasma Proteins in Amyotrophic Lateral Sclerosis Patients. *Int J Mol Sci.* 2023; 24(3):1899.
96. Baracaldo-Santamaría D., Avendaño-Lopez S.S., Ariza-Salamanca D.F., Rodriguez-Giraldo M., Calderon-Ospina C.A., González-Reyes R.E., Nava-Mesa M.O. Role of Calcium Modulation in the Pathophysiology and Treatment of Alzheimer's Disease. *Int J Mol Sci.* 2023; 24(10):9067.
97. Lucignani G., Salvatore M. Biotechnology in molecular and cellular imaging (344 visite). *International Journal Of Environmental Research And Public Health.* 2023; 20:793-805.
98. Blasiak J., Sobczuk P., Pawlowska E., Kaarniranta K. Interplay between aging and other factors of the pathogenesis of age-related macular degeneration. *Ageing Research Reviews.* 2022:101735.
99. Fang Y. Enabling Oligonucleotide-Based Therapeutics for Non-Liver Disease Targets. *Northeastern University.* 2023.
100. Futane A., Narayanamurthy V., Jadhav P., Srinivasan A. Aptamer-based rapid diagnosis for point-of-care application. *Microfluid Nanofluid.* 2023; 27(2):15.
101. Dong Y. Introduction of food integrity and aptamer-based analytical methods. *Aptamers for Food Applications: Elsevier.* 2023; 1-28.
102. Gu Z., Da Silva C.G., Hao Y., Schomann T., Camps M.G., van der Maaden K. et al. Effective combination of liposome-targeted chemotherapy and PD-L1 blockade of murine colon cancer. *Journal of Controlled Release.* 2023; 353:490-506.
103. Li H., Li Y., Li W., Cui L., Huang G., Huang J. A carbon nanoparticle and DNase I-Assisted amplified fluorescent biosensor for miRNA analysis. *Talanta.* 2020; 213: 120816.

104. Panigaj M., Johnson MB., Ke W., McMillan J., Goncharova EA., Chandler M., Afonin KA. Aptamers as modular components of therapeutic nucleic acid nanotechnology. In: Afonin KA (Ed.). *Therapeutic RNA Nanotechnology.* 2021:825-882.
105. Chan KY., Kinghorn AB., Hollenstein M., Tanner JA. Chemical modifications for a next generation of nucleic acid aptamers. *ChemBioChem.* 2022; 23(15):e202200006.
106. Kelly L., Maier KE., Yan A., Levy M. A comparative analysis of cell surface targeting aptamers. *Nature Communications.* 2021; 12(1):6275.
107. Di Mauro V., Lauta FC., Modica J., Appleton SL., De Franciscis V., Catalucci D. Diagnostic and Therapeutic Aptamers: A Promising Pathway to Improved Cardiovascular Disease Management. *JACC: Basic to Translational Science.* 2023.
108. Abdollahzade A., Rahimi H., Yaghoobi E., Ramezani M., Alibolandi M., Abnous K., Taghdisi SM. Targeted delivery of doxorubicin and therapeutic FOXM1 aptamer to tumor cells using gold nanoparticles modified with AS1411 and ATP aptamers. *Iranian Journal of Basic Medical Sciences.* 2023; 26(10):1177.
109. Odeh F., Nsairat H., Alshaer W., Ismail MA., Esawi E., Qaqish B. et al. Aptamers chemistry: Chemical modifications and conjugation strategies. *Molecules.* 2019; 25(1):3.
110. Chehelgerdi M., Chehelgerdi M., Allela OQB., Pecho RDC., Jayasankar N., Rao DP. et al. Progressing nanotechnology to improve targeted cancer treatment: overcoming hurdles in its clinical implementation. *Molecular Cancer.* 2023; 22(1):169.
111. Pishavar E., Yazdian-Robati R., Abnous K., Hashemi M., Ebrahimian M., Feizpour R. et al. Aptamer-functionalized mesenchymal stem cells-derived exosomes for targeted delivery of SN38 to colon cancer cells. *Iranian Journal of Basic Medical Sciences.* 2023; 26(4):388.
112. Yi K., Rong Y., Huang L., Tang X., Zhang Q., Wang W. et al. Aptamer–exosomes for tumor theranostics. *ACS Sensors.* 2021; 6(4):1418-1429.
113. Mehtani D., Seth A., Sharma P., Maheshwari N., Kapoor D., Shrivastava SK., Tekade RK. Biomaterials for sustained and controlled delivery of small drug molecules. In: Shukla A, Tripathi T (Eds.). *Biomaterials and Bionanotechnology.* Elsevier; 2019:89-152.

التطورات والعقبات المرتبطة بالاستراتيجيات العلاجية والتشخيصية المعتمدة على الأبتاميرات عبر مجالات طبية متنوعة: دراسة شاملة ومعمقة

أحمد سعد عبدالباري علي اغا[1]، ولهان الشاعر[2]، طلال ابورجيع[1*]

[1] كلية الصيدلة، قسم العلوم الصيدلانية، الجامعة الأردنية، عمان، الأردن.

[2]مركز العلاج بالخلايا، الجامعة الأردنية، عمان، الاردن.

ملخص

تُعتبر الأبتاميرات، وهي جزيئات من الحمض النووي الريبوزي المنقوص الأكسجين أو الحمض النووي الريبوزي، أدوات مهمة تكتسب شهرة متزايدة في مجالات التشخيص والعلاج في تخصصات طبية متنوعة مثل علم الأورام، الأمراض الرئوية، والاضطرابات العصبية. تقدم هذه الدراسة تقييمًا شاملًا للتطورات الأخيرة والتحديات التي تُواجهها مجالات تطبيقات الأبتاميرات. لقد أظهرت الأبتاميرات فعالية في الكشف المبكر عن السرطان وفي التوصيل الهدفي للعقاقير، مُقللةً من التأثيرات الجانبية. وتُبدي الأبتاميرات إمكانات كبيرة في إدارة الربو ومرض الانسداد الرئوي المزمن، من خلال استهداف السيتوكينات وتنظيم الاستجابة الالتهابية. تُقدم وسائل جديدة لإدارة الاضطرابات العصبية بفضل تأثيرها على علاقة الأمعاء والدماغ. رغم هذه الفوائد، لا تزال هناك تحديات مُستمرة تتعلق بالاستقرار الجزيئي وآليات التوصيل والجدوى الاقتصادية. تسلط هذه الدراسة الضوء على الجوانب المُتعددة لتطبيقات الأبتاميرات في التشخيص والعلاج، وتقدم نظرة شاملة للبحوث المستقبلية المُحتملة.

الكلمات الدالة: العلاج بالآبتامير؛ آبتاميرات التشخيص؛ تعديل المناعة؛ علاقة الدماغ–الأمعاء؛ مؤشرات خاصة بالأورام.

[*] ***المؤلف المراسل: طلال ابورجيع***

aburjai@ju.edu.jo

تاريخ استلام البحث 2023/10/21 وتاريخ قبوله للنشر 2024/1/30.