November - February 2020; 8(5): 1-9

International Journal of Research and Development in Pharmacy & Life Science
International open access peer-reviewed journal
ISSN (P): 2393-932X, ISSN (E): 2278-0238
Journal homepage: http://ijrdpl.com

Review Article

Aptamers: Trending Prospective in Therapeutics

Syed Abul Kalam*, Afreen Hashmi and Pranati Srivastava

Amity Institute of Pharmacy, Amity University Uttar Pradesh, Lucknow Campus, India

Keywords: SELEX, Chemical antibody, Chronic diseases, Bio-production, Targeting

Article Information:

Received: October 01, 2020;
Revised: January 01, 2020;
Accepted: February 01, 2020
Available online on:
15.02.2020@http://ijrdpl.com

http://dx.doi.org/10.47128/IJRDPL.2278-0238.2019.8(5).1-9

ABSTRACT: Aptamers are short stretches of Ribonucleic acid or Deoxyribonucleic acid having a specific 3D shape which form complexes with the target site with high affinity. Systemic Evolution of Ligands by Exponential Enrichment (SELEX) is responsible for the high affinity and specificity of aptamers to bind the target molecules. Due to some unique features of Aptamers, it attracts the attention of many scientists to use them as a tool in the treatment & diagnosis of various diseases and syndromes. The results obtained from the various clinical data shows that Aptamers can be used in the treatment and diagnosis of various diseases including cancer and syndromes like AIDS, severe acute respiratory syndrome etc. Many viral infections like human immunodeficiency virus, hepatitis B virus and Ebola virus are now treated or diagnosed with the help of aptamers. Along with viral infections, aptamers are also promising Chemical antibodies in the treatment of various kinds of cancer like breast cancer, lung cancer, colorectal cancer, etc. Aptamers have several advantages over conventional antibodies in context to its size, thermal stability, immunogenicity, ease of modification, etc. Aptamers are smaller than conventional antibodies, this property allows aptamers to access in tissue and cell. Aptamers are synthetic agents and we scale up its production as per requirement and it eliminate the various regulatory requirements associated with bio-production. The various roles of aptamers in the treatment and diagnosis of many life-threatening diseases, syndromes and viral infections like cancer, AIDS, Ebola virus lead aptamers to serve as Future Pharmaceutical dosage form or prospective Future of Modern Medical Science.

⇑ Corresponding author at:
Syed Abul Kalam, Amity Institute of Pharmacy, Amity University Uttar Pradesh, Lucknow Campus, India
E-mail: abulbbdu@gmail.com

INTRODUCTION

Aptamers are the short stretches of ribonucleic acid/ deoxyribonucleic acid having an ability to bind with the specific target sites/molecules with high affinity. These new agents are 3D in shape and used for diagnostic, therapeutic purpose and as a carrier to deliver drug to the target site.

This versatile nature of aptamers attracts the attention of many scientists to use aptamer as an attractive tool in a large array of biological applications. Aptamers are the unique molecule which performs several functions-

- ✓ As a drug molecule which targets the structural sites which are responsible for disease conditions.
- ✓ As a chemical antibody.
- ✓ As a drug carrier to deliver drug on target sites.
- ✓ Diagnostic applications

Aptamers are also regarded as “chemical antibodies”, synthesized in laboratory and serve as an alternative of conventional antibodies. These chemical agents have an ability to overcome the limitations of antibodies [1].

Advantages of Aptamers over Conventional Antibodies

High Stability: Proteins are thermo labile and denatured in high temperature and ultimately lose their specific 3D structure while oligonucleotide-based aptamers are more thermo stable and have a capacity to maintain their specific 3D structure continuous cycle of denaturation & renaturation. Aptamers bind to the target site after re-annealing while conventional antibodies irreversibly denatured. The stability and nuclease resistance of aptamers can be easily enhanced by several chemical reactions.

***In vitro* Production:** The *in vitro* production of monoclonal antibodies is much more expensive and their identification requires screening of several batches of colonies. One of the limitations of these monoclonal antibodies is that they require immunoassay to ensure the effectiveness of these antibodies in each batch while aptamers are synthetic molecules and synthesized in large quantity with high accuracy and precision that's why the production cost of aptamers is less than the antibodies.

Immunogenicity: These chemical antibodies are less immunogenic and less toxic in comparison to conventional antibodies. The low immunogenicity of aptamers is due to the chemical nature (i.e. nucleic acid). The human immune systems don't have an ability to recognized these nucleic acids as foreign agent.

Variety of Targets: Those molecules which cannot be identified with the conventional antibodies like ions and small molecules, aptamers can easily bind to these molecules with high affinity and specificity [2]. The distinguished features represent in Table 1.

Table 1: Difference between Aptamers and Conventional Antibodies [3-6]

S. No.	Parameter	Conventional Antibodies	Aptamers
1	Chemical Nature	Polymer peptide	Nucleic acid
2	Specificity	Good	Good
3	Affinity	Good	Good
4	Immunogenicity	High	No humeral response
5	Production	Bio-production	Synthetic
6	Cost	Expensive	Cheap
7	Stability	Low	High
8	Potential Targets	Limited to Immunogenic molecule	Wide range
9	Generation Time	Approx. 150-180 Days	Approx. 21-50 days
10	Ease of Modification	Complex	Easily modified

Limitations of Aptamers

1. Aptamers degradation by nucleases in biological media
2. Aptamers excreted from the blood stream by renal filtration
3. Controlling the duration time of action
4. Aptamer interacts with intracellular targets
5. Target proteins are required for the synthesis of desired aptamer
6. Aptamers cross-reactivity
7. Require highly skilled person for aptamer generation [7]

Selection & Isolation of desired Aptamers (SELEX Technique)

SELEX, an advanced technique of selecting desired aptamers which possess high affinity for a specific target site from approximately 10^{11}-10^{16} Oligonucleotide Pools (IOP). It is a process of selecting or isolating desired aptamer from a library of aptamers. It involves three basic steps which can be repeated several times in order to find desired aptamer.

Primary Step: Library generation

Secondary Step: Binding and separation

Tertiary Step: Amplification

Library Generation In this step initial oligonucleotide pool (IOP) is incubated with a target molecule. These initial oligonucleotide pools also known as "Combinatorial libraries".

Binding and Separation In secondary stem the target bounded components are separated from unbounded library components.

Amplification In tertiary step the bounded components are amplified by the polymer chain reaction (PCR) to generate a new library which is to be further used [8-9].

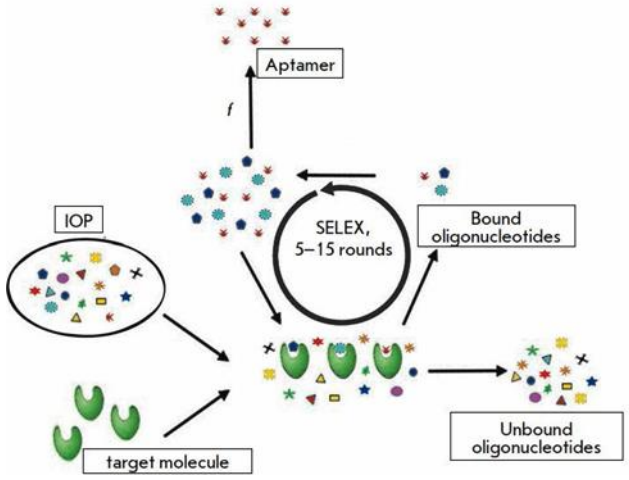

Fig. 1: Process of SELEX [2]

Types of SELEX Process

1. Nitrocellulose membrane filtration-based SELEX
2. Affinity chromatography and magnetic bead-based SELEX
3. Capillary- Electrophoresis Based SELEX
4. Microfluidic based SELEX
5. Cell SELEX [10]

***Diagnostic Applications*:** The high affinity of the aptamer towards their target molecules lead aptamer to serve as a potential tool in diagnostic field. In 1999 the first aptamer used in diagnosis was developed by Bruno, who detect anthrax spores but now a days several aptamers-based techniques are developed to diagnose ophthalmic, cardiovascular and cancer disease with high accuracy. These aptamers based diagnostic agent contain aptamer and a fluorescent/radionuclide for signaling [11]. Several examples put in Table 2.

Applications of Aptamers

Table 2: Example of Aptamers which utilized in diagnosis

Aptamer	Target site	Kd[nM]	Sensitivity	Specificity	Reference
In Cancer					
Aptamer XL 33	Metastatic Colorectal Cancer	0.7	81.70%	66.70%	[12]
Aptamer LXL 1	Metastatic breast cancer cells	44.00	76.00%	100%	[13]
Aptamer SYL3-C	Solid Cancer Epithelial Cell Adhesion Molecule	22.30	60%	100%	[14-15]
In CVS Diseases					
Aptamer Myo040-7-27	Myoglobin	4.93	10pm	-	[16]
In Infectious Disease					
Aptamer LmWC-25R and LmHSP-7b/11R	Leishmania promastigote & hydrophilic surface protein	-	100 ng	-	[17]
Aptamer 2008s	Plasmodium falciparum lactate dehydrogenase enzyme	42-59	57ng/mL	No human LDH recognition	[18]

***ALISA (Aptamer linked Immobilized Sorbent Assay)*:** Enzyme linked Immuno sorbent Assay (ELISA) is one of the major techniques used for the detection of HIV, not only HIV but almost any peptide or protein molecule can be detected with high affinity. Sandwich ELISA which involves using 2 antibodies or analyte-binding receptor proteins to bind the target molecule. ALISA technique was introduced by Kiel, who demonstrate the feasibility of ALISA in comparison to ELISA using antibody, which shows that aptamers have an ability to overcome the limitations of antibodies.

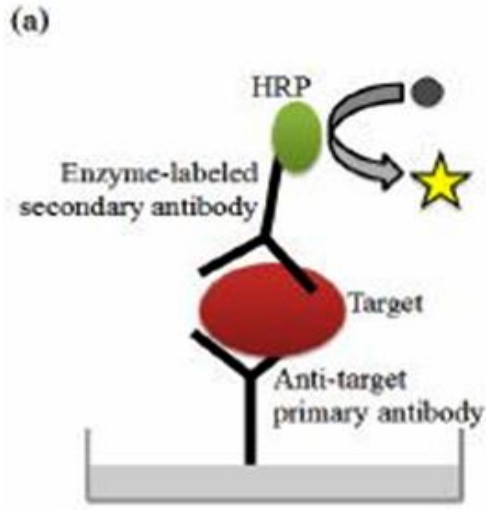

Fig. 2(a): the ELISA technique

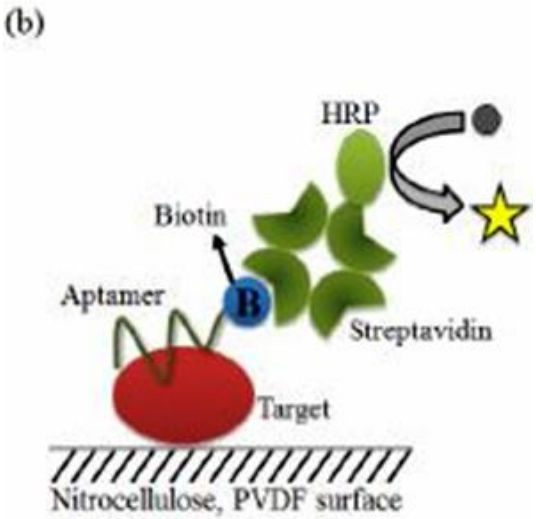

Fig. 2(b) the ALISA technique [1]

***Western Blot Analysis*:** A western blot analysis is an advanced analytical approach used to identify specific proteins from a sample. This test requires two types of antibodies to quantify specific proteins. Hah's group demonstrate the aptamer based Western blot analytical approach which reduces the time and cost by employing only one aptamer to quantific specific protein in place of two antibodies. Different diagnostic methods mention in Table 3.

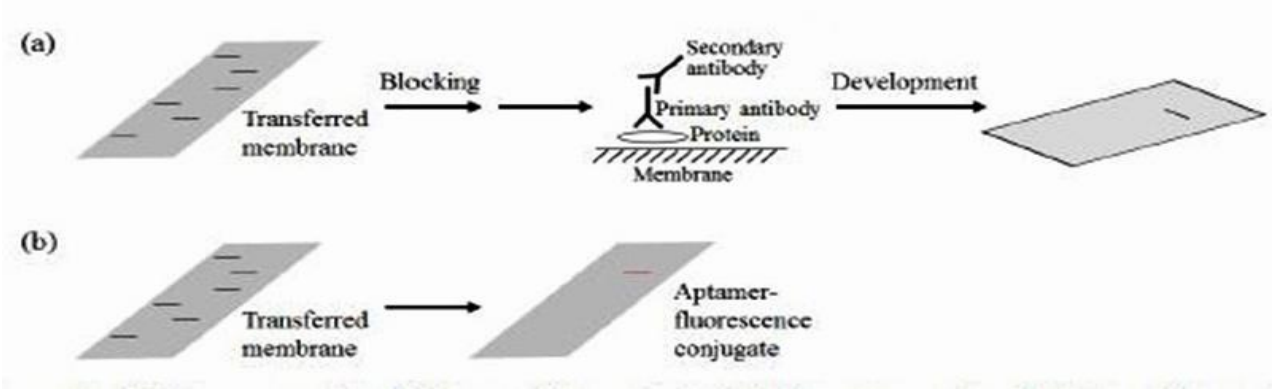

Fig. 3(a): Conventional Western blot Analysis, (b) Aptamer based Western blot analysis [1]

Table 3: Comparison of different diagnostic techniques

Name of the Virus	Technique	Detection Limit	Advantages	Disadvantages	References
Influenza	Isolation & Identification of the virus	l EID50/ml	Good Sensitivity	Time taking process	[19]
	ELISA	l.0mg	Quick Result	The chances of false positive result are high.	[20]
	Reverse Transcriptase Polymer Chain Reaction [RT-PCR]	0.0256 HAU	Provide high specificity and sensitivity	Expensive and complicated process require highly skilled person	[21]
	qRT-PCR	10 copies/reaction			[22]
HBV	ELISA	0.5pg/mL	Specificity Sensitivity	Expensive and complicated process require highly skilled person	[23]
	qRT-PCR	18 IU/mL			[24]
HIV	ELISA	0.9-1.2 IU/mL	Specificity Sensitivity	Expensive complicated, require highly skilled staff	[25]
	qPCR	18-65 copies/mL			[26]

There are various methods available to detect Influenza virus but Surface Plasmon Resonance Aptamers [SPR Aptamer] diagnose this virus in less time (i.e.1.5 hour) in comparison to other methods like ELISA, RT-PCT etc with high specificity & sensitivity. Detection time comparison with diagnostic method mention in Table 4.

Table 4: Comparison of detection time of Avian Influenza Virus with different Diagnostic method [27]

Method	Virus Isolation	ELISA	RT-PCT	qRT-PCR	SPR Aptamers
Detection time	5-7 days	3 hours	5 hours	3 hours	1.5 hour

Bio-imaging: Bio-imaging is non-invasive process of visualizing biological process in real time. In this aptamer is conjugated with a fluorophore, a Quantum Dots or Gadolinium, which is useful in Magnetic Resonance Imaging. The advantage of aptamer in Bio-imaging is its fewer toxic properties because of its oligonucleotide nature. Another advantage is its high specificity for their fast diffusing capacity through systemic circulation. The QD-A10 and DUP-1 named aptamer complex are highly specific for Prostate Specific Membrane Antigen or PSMA [+] and PSMA [-] and binds to the prostate cancer cell not any other normal or cancerous cell [28].

Several other aptamers are demonstrated to specific for P68 in liver tumor and an aptamer specific for small cell lung cancerous cell was demonstrated to be used as bio imaging probe [29-31].

Therapeutic Applications

1. ***Age related Macular Degeneration (AMD)***

Macugen is a Ribonucleic acid aptamer which consist of 180 nucleotide and commercially marketed as "**Pegaptanib**". Pegaptanib was the first aptamer approved in 2004 by Federal Drug Administration for the treatment of AMD [32]. Age related Macular degeneration is an eye disease in which the abnormal blood vessels are formed which are excessively leakage and may cause blindness in the absence of treatment. The initial version of macugen was developed by NeXstar Pharmaceutical and then the licence was sold to EyeTech Company in 2000 for further development in U.S. Pfizer markets macugen outside the United States. The molecular weight of macugen is 50 kDa and Molecular formula is $C_{29}4H_{342}F_{13}Na_{107}O_{188}P_{28}$ $(C_2H_{40})2n$ (n=900) with biological half-life of 10 days.

Mechanism of Action: Macugen bind to l65 isoform of VEGF and inhibit its interaction vascular endothelial factor receptor present on blood vessels in eyes, it also prevents the formation of abnormal blood vessels and finally reduces the swelling on eyes [33].

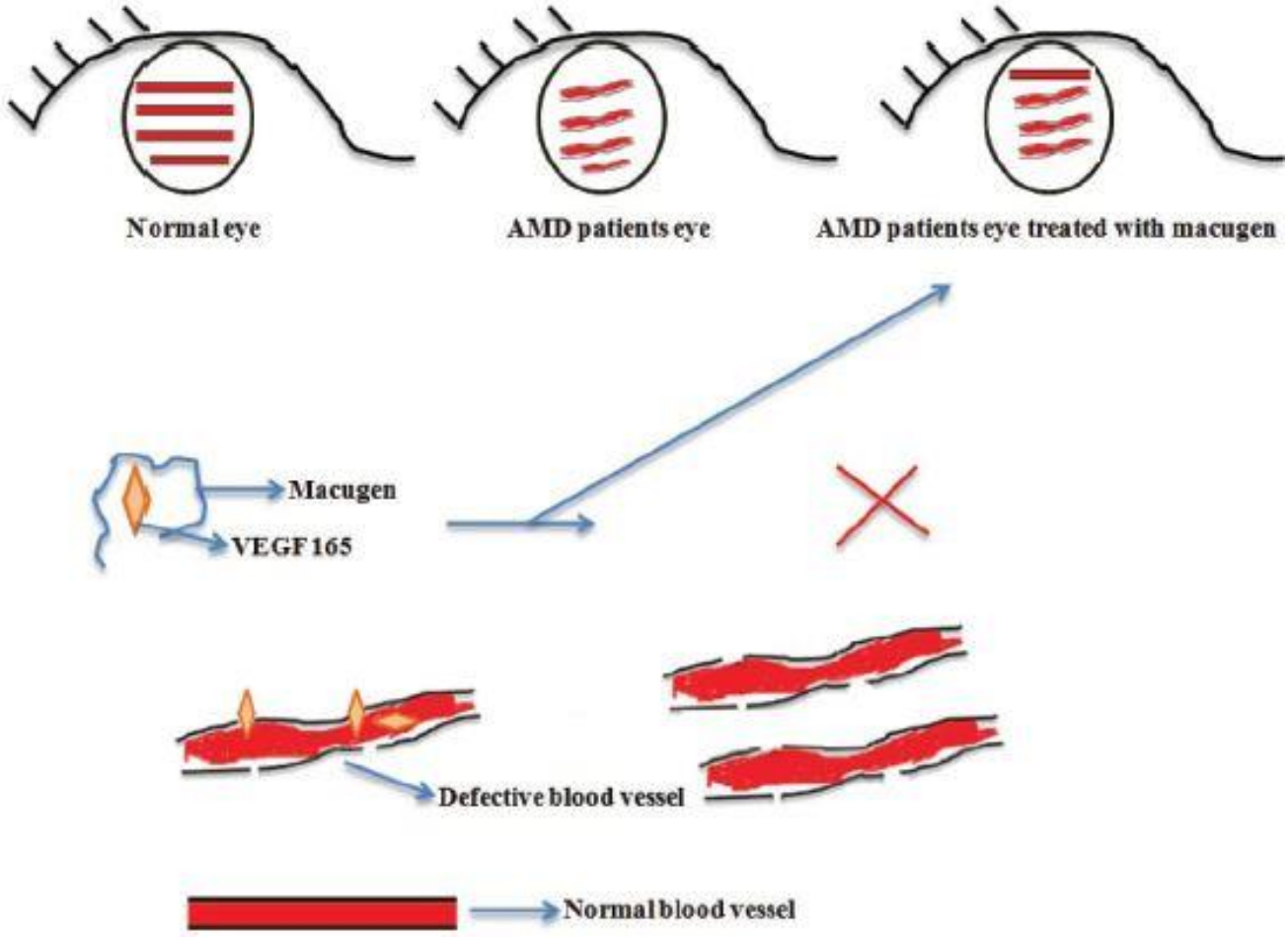

Fig. 4 - Macugen for AMD treatment [33]

2. *Anti-Obesity Aptamers*

Obesity is a worldwide problem due to current life style. Spiegelmer is a L-aptamer developed by NOXXON Company and used against ghrelin to treat obesity. Ghrelin is a peptide hormone which responsible for appetite and weight gains. The results obtained from animal studies show the anti-obesity property of Spiegelmer [34].

3. *Aptamers in Cancer Treatment*

Activation of oncogenes and deactivation of tumor suppressing genes alter the normal physiology of proliferation and apoptosis and may lead to form tumor or cancer [35].

(i) Aptamers against VEGF and Platelet Derived Growth Factor

Macugen was the first Federal Drug Administration approved Ribonucleic Acid aptamer, commercially known as Pegaptanib used for the treatment of AMD and act by inhibiting the binding of vascular endothelial growth factor to its receptor [36]. Macugen was then used in the anti-angiogenesis therapy and Pegaptanib become promising agent in cancer treatment. However alone anti-vascular endothelial growth factor is not sufficient to inhibit new blood vessel formation in the deviant angiogenesis.

This problem occurs due to the roles of Platelet-derived growth factor-B signaling in angiogenesis. This fact is well established that PDGF-B binding to its receptor accelerate the vessel maturation and it also stable the new blood vessels [37].

The results obtained from clinical studies shows that selective inhibition of VEGF receptor resulted in the accumulation of mural cell to cancerous blood vessels and create a resistance to anti-VEGF receptor agent [38]. In order to overcome this resistance RTK inhibitors (SU6668) is used which target the VEGFR-2 and PDGF-B and significantly inhibit the brain tumor vessels prematurely [39].

(ii) Aptamers against Nucleolin and Stromal cell derived factor-1 ligand 12 (CXCL12)

NOX-A12 and AS1411 named aptamers are under clinical trial leukemia treatment. AS1411 is a guanine quodruplex based aptamer which bind to the nucleolin (overexpressed in cancer) inhibit the activation of NF-κB (Nuclear factor κB) and B-cell lymphoma II and ultimately sensitize the cancerous cells from chemotherapy [40].

The result obtained from various clinical data shows that AS1411 have a significant anti-tumor activity in cancer [41]. For treating cancer list of Aptamers given in Table 5.

Table 5: Aptamers in the treatment of Cancer

Aptamer (DNA/RNA)	Targets	Functions	Anti-tumor effect	References
Pegaptanib (Ribonucleic acid)	Vascular Endothelial Growth Factor – 165	Inhibition of abnormal vessels formation	Positive	[37]
Arc126/ax102 (Ribonucleic acid)	Platelet Derived Growth Factor-B	Inhibition of newly formed blood vessel growth	Positive	[42-43]
SL (2)- B/RNV66 (Deoxyribonucleic acid)	Vascular Endothelial Growth Factor -165	Inhibit Endothelial Growth Factor associated angiogenesis	Positive	[44-45]
PPAR-apt (Ribonucleic acid)	Peroxisome Proliferator Activated Receptor	Inhibits Peroxisome Proliferator Activated Receptor -dependent VEGF signals	Positive	[46]
AS1411 (Deoxyribonucleic acid)	Nucleolin	Inhibition of nucleolin-associated cell processes and Nuclear Factor-κB or Bcl-2 signaling	Positive	[47-48]
NOX-A12 (Ribonucleic acid)	Stomal cell-derived factor 1 (SDF1)	Inhibit SDF1-induced cell new vessel formation	Positive	[49-52]
A30 (Ribonucleic acid)	Human Epidermal Growth Receptor 3	Inhibition of HGR-dependent tyrosine phosphorylation of HER2 and MAPK signaling	Positive	[53]
E0727/CL428/KD1130 (Ribonucleic acid)	Endothelial Growth Factor Receptor	Inhibit Endothelial Growth Factor Receptor phosphorylation APK signaling	Positive	[54-58]

4. *Aptamers against Hiv*

The human immunodeficiency virus is a retrovirus which caused HIV infection and when CD4 cell count fall down and become less than 200, the condition called Acquired immune-deficiency syndrome (AIDS) .When CD4 cells of the infected person fall down into critical level, the cell mediated immunity is affected then the patient is more susceptible to other opportunistic infection. ART (Antiretroviral therapy) medications are used now a days and these medications decrease the viral replication rate. The disadvantage of these medication is its high cost and its severe adverse effect on body. In order to overcome these limitations aptamers have been considered an alternative for these toxic antiretroviral drugs. Aptamers are highly specific which targets the various part of Human-immune deficiency virus-1 genome and its proteins like protease, surface glycoprotein 120, reverse transcriptase and ultimately suppress the viral replications.

(i) Aptamer against Integrase- G-quodruplex containing aptamers have antiviral activity. The viral integrase enzyme is important for the Hiv replication, this integrase enzyme catalyze the integration of newly formed ds-viral DNA genome into the host genome. T30177 named aptamer which developed by Aronex Pharmaceuticals, USA have a property to inhibit integrase enzyme and ultimately suppress the viral replication. T30177 was the first clinically approved integrase inhibitor.

(ii) Aptamer against Gp120- Surface glycoprotein 120 play an important role in the Hiv entry into the cell. Gp120 helps in attachment of Hiv to CD4 cells. G-quodruplex containing aptamer targets gp120 and shows antiviral activity. ISIS-5320 was the first G-quodruplex containing aptamer which inhibit virus entry by forming tetrameric G-quodruplex structure and binds to the loop of glycoprotein 120.

(iii) Aptamers against Nucleocapsid- The Nucleocapsid protein of human immune deficiency virus-1 is essential for the encapsidation of viral particles and can be forbid by inhibiting the synthesis of nucleocapsid. Kim isolated the Ribonucleic acid aptamer which binds to the nucleocapsid and contest the packaging element ribonucleic acid binding. Kim also suggest that this Ribonucleic acid aptamer have a capacity to inhibit the viral packaging [59]. Selected aptamers against HIV listed in Table 6.

Table 6: Aptamers selected against HIV [60]

Aptamer	DNA/RNA	Target
ASn, ALn, BLn and BSn	Ribonucleic acid	LTR viral sequence
RNApt16	Ribonucleic acid	5'-untranslated regions of HIV-1 genome
PR10.9,PR10.18,PR10.1 and PR10.13	Ribonucleic acid	Protease viral protein
T30695 and T30177	Deoxyribonucleic acid	Integrase viral protein
37NT	Deoxyribonucleic acid	RT-viral protein
RT5, RT7 and RT 47	Deoxyribonucleic acid	RT-viral protein
ODNs 93 and 112 93del, 112del	Deoxyribonucleic acid	RNAse activity associated to RT-viral protein

Aptamers as a Drug Delivery System

Aptamers also have a capacity to deliver drug to their target sites. Most of the cell-based disease like cancer etc. requires drugs to be physically delivered to the desired site. Basically, these sites occur in intracellular and extracellular proteins, lipids and mitochondria. Aptamers which have a ability to bind with internalized cell surface receptors, has been use to deliver drug on desired site. Eg- The PSMA which is an important prostate cancer-marker. The two aptamers named A10 and DUP-1 are synthesized to target cancer cell and deliver anticancer drug (doxorubicin) to treat prostate cancer cell. Aptamers have a capacity conjugate therapeutic moiety in order to deliver drug to target site. Doxorubicin is an anticancer drug which covalently conjugate with AS1411 named DNA aptamer which have a high affinity for nucleolin protein which is overexpressed in many cancer [61]. Current scenario of Aptamers is mentioned in Table 7.

Table 7: R & D Status of Aptamers in Current Scenario [62]

Sr. No.	Name of the Aptamer	Form	Therapeutic uses	Current Status
1	Pegaptanib sodium	27-Nucleotide RNA	In the treatment of AMD	Approved by FDA
2	E10030	29-Nucleotide DNA	In the treatment of AMD	Phase- III
3	REG (RB007 & RB006)	37-Nucleotide RNA	In the treatment of Coronary artery disease	Phase-III
4	ARC 1905	38-Nucleotide RNA	In the treatment of AMD	Phase-III
5	AS1411	26-Nucleotide DNA	In the treatment of Acute myeloid Leukemia	Phase-II
6	ARC1779	39-Nucleotide DNA	In the treatment of Von Willebrand disease	Phase-II
7	NOX-E36	40-Nucleotide RNA	In the treatment of Chronic inflammatory disease	Phase-II
8	NOX-A12	45-ntRNA	In the treatment of Multiple myeloma & Hematopoietic stem cell transplantation	Phase-II
9	NU172	26-Nucleotide DNA	In the treatment of Heart Disease	Phase-II
10	NOX-H94	44-Nucleotide RNA	In the treatment of Anemia, inflammation & end-stage renal disease	Phase-II
11	ARC19499	32-Nucleotide RNA	In the treatment of Hemophilia	Phase-I

Future Prospective

Aptamers are special molecules and prospective as alternative of conventional antibodies. These molecules overcome the limitations of conventional antibodies in context to its size, stability, lack of immunogenicity and ease of production & modification. These properties make aptamers to serve as a potential tool to treat various kind of disease like age-related macular degeneration, cancer, HIV infection, obesity etc. Aptamers also play an important role in diagnostic field eg. Western Blot Analysis and ALISA. ALISA in an advanced technique and is highly comparable to ELISA. Aptamers also utilizes in bio-imaging because of its less toxic effect in comparison to conventional bio-imaging. Aptamers also used as a drug delivery system to deliver drugs to their target site. In current scenario only one aptamer is commercially available i.e. Macugen (Pegaptanib sodium injection) approved by Federal Drug Administration, used for the treatment of AMD but several other aptamers are also under clinical trial. The various role of aptamer in the treatment and diagnosis of many life-threatening disease leads aptamer to serve as a prospective future pharmaceutical drug.

ACKNOWLEDGMENT

The authors are grateful to Amity Institute of Pharmacy, Amity University Uttar Pradesh for facilitating this work.

REFERENCES

1. Kyung MS, Seonghwan L, Changill B. Aptamers and Their Biological Applications. Sensors. 2012; 12: 612-631.
2. Lakhin AV, Tarantul VZ, Gening LV. Aptamers: Problems, Solutions and Prospects. Acta Naturae. 2013; 5(4): 34-41.
3. Mascini M. Aptamers and their applications. *Anal. Bioanal. Chem.* 2008; 390: 987–988.
4. Birch J R, Rache A J. Antibody production. *Adv. Drug. Deliv. Rev.* 2006; 58: 671–685.
5. Ferreira CS, Missailidis S. Aptamer-based therapeutics and their potential in radiopharmaceutical design. *Braz. Arch. Biol. Technol.* 2007; 50: 63–76.
6. Jayasena S D. Aptamers: An emerging class of molecules that rival antibodies in diagnostics. *Clin. Chem.* 1999; 45: 1628–1650.
7. Ireson C R, Kelland L R. Discovery and development of anticancer aptamers. *Mol. Cancer. Ther.* 2006; 5: 2957–2962.
8. Zhenjian Z, Yuanyuan Y, Maolin W, Jie L, Zongkang Z, Jin L, Xiaohao W. Recent Advances in SELEX Technlogy and Aptamer Applications in Biomedicine. *Int. J. Mol. Sci.* 2017; 18: 1-13.

9. Syed M A, Pervaiz S. Advances in aptamers. Oligonucleotides. 2010; 20: 215–224.
10. Bruno JG, Kiel JL. *In vitro* selection of DNA aptamers to anthrax spores with electrochemiluminescence detection. *Biosens. Bioelectron*. 1999; 14: 457–464.
11. Wan Y, Kim YT, Li, N, et al. Surface-immobilized aptamers for cancer cell isolation and microscopic cytology. *Cancer. Res.* 2010; 70: 9371–9380.
12. Li X, An Y, Jin J, Zhu Z, Hao L, Liu L, Shi Y, Fan D, Ji T, Yang CJ. Evolution of DNA aptamers through *in vitro* metastatic-cell-based systematic evolution of ligands by exponential enrichment for metastatic cancer recognition and imaging. *Anal. Chem.* 2015; 87: 4941–4948.
13. Li X, Zhang W, Liu L, Zhu Z, Ouyang G, An Y, Zhao C, Yang, CJ. *In vitro* selection of DNA aptamers for metastatic breast cancer cell recognition and tissue imaging. *Anal. Chem.* 2014; 86: 6596–6603.
14. Song Y, Zhu Z, An Y, Zhang W, Zhang H, Liu D, Yu C, Duan W, Yang CJ. Selection of DNA aptamers against epithelial cell adhesion molecule for cancer cell imaging and circulating tumor cell capture. *Anal. Chem*. 2013; 85: 4141–4149.
15. Ji WK, Eun YK, Sun YK, et. al. Identification of DNA Aptamers Toward Epithelial Cell Adhesion Molecule via cell-SELEX. Mol Cells . 2014 Oct 31;37(10):742-6.
16. Wang Q, Liu W, Xing Y, Yang X, Wang K, Jiang R, Wang P, Zhao Q. Screening of DNA aptamers against myoglobin using a positive and negative selection unit integrated microfluidic chip and its biosensing application. *Anal. Chem.* 2014; 86: 6572–6579.
17. Bruno JG, Richarte AM, Phillips T, Savage AA, Sivils JC, Greis A, Mayo MW. Development of a fluorescent enzyme-linked DNA aptamer-magnetic bead sandwich assay and portable fluorometer for sensitive and rapid leishmania detection in sandflies. *J. Fluoresc.* 2014; 24: 267–277.
18. Cheung YW, Kwok J, Law AW, Watt RM, Kotaka M, Tanner JA. Structural basis for discriminatory recognition of plasmodium lactate dehydrogenase by a DNA aptamer. *Proc. Natl. Acad. Sci.* 2013; 110: 15967–15972.
19. Charlton B, Crossley B, Hietala S. Conventional and future diagnostics for avian influenza. *Comp. Immunol. Microbiol. Infect. Dis.* 2009; 32: 341–350.
20. Luo Q, Huang H, Zou W, Dan H, Guo X, Zhang A, Yu Z, Chen H, Jin M. An indirect sandwich ELISA for the detection of avian influenza H5 subtype viruses using anti-hemagglutinin protein monoclonal antibody. *Vet. Microbiol.* 2009; 137: 24–30.
21. Dhumpa R, Handberg KJ, Jørgensen PH, Yi S, Wolff A, Bang DD. Rapid detection of avian influenza virus in chicken fecal samples by immunomagnetic capture reverse transcriptasepoly-merase chain reaction assay. *Diagn. Microbiol. Infect. Dis.* 2011; 69: 258–265.
22. Sidoti F, Rizzo F, Costa C, Astegiano S, Curtoni A, Mandola ML, Cavallo R, Bergallo M. Development of real time RT-PCR assays for detection of type A influenza virus and for subtyping of avian H5 and H7 hemagglutinin subtypes. *Mol. Biotechnol.* 2010; 44: 41–50.
23. Yang J, Kim JH, Kim Y. Comparison of nine different qualitative HBsAg assay kits. *Korean. J. Lab. Med.* 2010; 30: 178–184.
24. Kim H, Shin S, Oh EJ, Kahng J, Kim Y, Lee HK, Kwon HJ. Comparison of the AdvanSure HBV real-time PCR test with three other HBV DNA quantification assays. *Ann. Clin. Lab. Sci.* 2013; 43: 230–237.
25. Muhlbacher A, Schennach H, Helden J, Hebell T, Pantaleo G, Bürgisser P, Cellerai C, Perm-pikul P, Rodriguez MI, Eiras A. Performance evaluation of a new fourth-generation HIV combination. *Med. Microbiol. Immunol.* 2013; 202: 77–86.
26. Saune K, Delaugerre C, Raymond S, Nicot F, Boineau J, Pasquier C, Izopet J. Analytical sensitivity of three real-time PCR assays for measuring subtype B HIV-1 RNA. *J. Clin. Virol.* 2013; 57: 80–83.
27. Tomasz W, Joanna W, Piotr K. Aptamers in Diagnostics and Treatment of Viral Infections. Viruses. 2015; 7: 751-780.
28. Min K, Song KM, Cho M, et al. Simultaneous electrochemical detection of both PSMA (+) and PSMA (−) prostate cancer cells using an RNA/peptide dual-aptamer probe. *Chem. Commun.* 2010; 46: 5566–5568.
29. Bagalkot V, Zhang L, Levy-Nissenbaum E, et al. Quantum dot-aptamer conjugates for synchronous cancer imaging, therapy, and sensing of drug delivery based on bi-fluorescence resonance energy transfer. *Nano. Lett.* 2007; 7: 3065–3070.
30. Kunii T, Ogura S, Mie M, et al. Selection of DNA aptamers recognizing small cell lung cancer using living cell-SELEX. Analyst. 2011; 136: 1310–1312.
31. Mi J, Liu YM, Rabbani ZN, et al. In vivo selection of tumor-targeting RNA motifs. *Nat. Chem. Biol.* 2010; 6: 22–24.
32. Ng EWM, Shima DT, Calias P, et al. Pegaptanib, a targeted anti-VEGF aptamer for ocular vascular disease. *Nat. Rev. Drug. Discov*. 2006; 5: 123-32.
33. Kourlas H, Schiller D S. Pegaptanib sodium for the treatment of neovascular age-related macular degeneration: A Review. *Clinical. Ther.* 2006; 28: 36-44.
34. Abhishek P. Aptamers in Therapeutics. JCDR. 2016; 10(6): 1-5.
35. Gang Z, George W, Lionel H, et al. Aptamers: A promising chemical antibody for cancer therapy. Oncotargets. 2015; 7(12): 13446-13458.
36. Muhammed A, Kwang G. Drug-target network. *Nat. Biotechnol.* 2007; 25: 1119-1126.
37. Ng EW, Shima DT, Calias P, et al. Pegaptanib, a targeted anti-VEGF aptamer for ocular vascular disease. *Nat. Rev. Drug. Disco*v. 2006; 5: 123-132.
38. Alvarez R H, Kantarjian H M, Cortes J E. Biology of plateletderived growth factor and its involvement in disease. *Mayo. Clin. Proc*. 2006; 81: 1241-1257.
39. Jo N, Mailhos C, Ju M, et al. Inhibition of plateletderived growth factor B signaling enhances the efficacy of anti-vascular enclothelial growth factor therapy in multiple models of ocular neovascularization. *Am. J. Pathol.* 2006; 168: 2036-2053.
40. Cahristdropher R I, Lloyd R K. Discovery and development of anticancer aptamers. *Mol. Cancer. Ther*. 2006; 5: 12-24.

41. Bates PJ, Laber DA, Miller DM, et al. Discovery and development of the G-rich oligonucleotide AS1411 as a novel treatment for cancer. *Exp. Mol. Pathol*. 2009; 86: 151-164.
42. Akiyama H, Kachi S, Silva RL, et al. Intraocular injection of an aptamer that binds PDGFB: a potential treatment for proliferative retinopathies. *J. Cell. Physiol.* 2006; 207: 407-412.
43. Sennino B1, Falcón BL, McCauley D, et al. Sequential loss of tumour vessel pericytes and endothelial cells after inhibition of platelet-derived growth factor B by selective aptamer AX102. *Cancer. Res.* 2007; 67: 7358-7366.
44. Kaur H, Li J J, Bay B H. Investigating the anti-proliferative activity of high affinity DNA aptamer on cancer cells. PLoS On 2013; 8: e50964.
45. Stacey LE, Vasanthanathan P, Jagat RK, et al. Targeting VEGF with LNA-stabilized G-rich oligonucleotide for efficient breast cancer inhibition. *Chem. Commun*. 2015; 51: 9499-9502.
46. Kwak H, Hwang I, Kim JH, et al. Modulation of transcription by the peroxisome proliferatoractivated receptor δ-binding RNA aptamer in colon cancer cells. *Mol. Cancer. Ther*. 2009; 8: 2664-2672.
47. Cahristdropher R I, Lloyd R K. Discovery and development of anticancer aptamers. *Mol. Cancer. Ther.* 2006; 5: 12-24.
48. Mongelard F, Bouvetety P. AS 1411, a guanosine rich oligo¬nucleotide aptamer targeting nucleolin for the potential treatment of cancer, including acute myeloid leukemia. *Curr. Opin. Mol. Ther.* 2010; 12: 107-114.
49. Vater A, Sahlmann J, Kroger N, et al. Hematopoietic stem and progenitor cell mobilization in mice and humans by a first-in-class mirror-image oligonucleotide inhibitor of CXCL12. *Clin. Pharmacol. Ther.* 2013; 94: 150-157.
50. Liu SC, Alomran R, Chernikova SB, et al. Blockade of SDF-1 after irradiation inhibits tumor recurrences of autochthonous brain tumors in rats. *Neuro. Oncol*. 2014; 16: 21-28.
51. Hinterseer E. The spiegelmer NOX-A12 abrogates homing of human CLL cells to bone marrow and mobilizes murine CLL cells in the Eu-TCL1 transgenic mouse model of CLL. *American Society of Hematology*. 2013; 41: 11-16.
52. Hoellenriegel J, Zboralski D, Maasch C, et al. The spiegelmer NOX-A12, a novel CXCL12 inhibitor, interferes with chronic lymphocytic leukemia cell motility and causes chemosensitization. Blood. 2014; 123: 1032-1039.
53. Chen CH, Chernis GA, Hoang VQ, et al. Inhibition of heregulin signaling by an aptamer that preferentially binds to the oligomeric form of human epidermal growth factor receptor-3. *Proc. Natl. Acad. Sci.* 2003; 100: 9226-9231.
54. Li N, Nguyen HH, Byrom M, et al. Inhibition of cell proliferation by an anti-EGFR aptamer. PLoS One. 2011; 6: e20299.
55. Esposito CL, Passaro D, Longobardo I, et al. A neutralizing RNA aptamer against EGFR causes selective apoptotic cell death. PLoS One. 2011; 6: e24071.
56. Wan Y, Tamuly D, Allen PB, et al. Proliferation and migration of tumor cells in tapered channels. *Biomed. Micro.* 2013; 15: 635-643.
57. Buerger C, Nagel WK, Kunz C, et al. Sequence-specific peptide aptamers, interacting with the intracellular domain of the epidermal growth factor receptor, interfere with Stat3 activation and inhibit the growth of tumor cells. *J. Biol. Chem.* 2003; 278: 37610- 37621.
58. Wang DL, Song YL, Zhu Z, et al. Selection of DNA aptamers against epidermal growth factor receptor with high affinity and specificity. *Biochem. Biophys. Res. Commun*. 2014; 453: 681-685.
59. Jyoti B, Srinivasan C, Rajib KD, et. al. Aptamers in HIV research diagnosis and therapy.RNA Biol. 2018; 15(3): 327–337.
60. Victor MG, Elena MM, Geronima F, Ana GS. Use of Aptamers as Diagnostics Tools and Antiviral Agents for Human Viruses. Pharmaceuticals. 2016; 9(78): 1-24.
61. Partha R, Rebekah R.W. Aptamers for Targeted Drug Delivery. Pharmaceuticals (Basel). 2010 Jun; 3(6): 1761–1778.
62. Zhenjian Z, Yuanyuan Y, Maolin W, Jie L, Zongkang Z, Jin L, Xiaohao W. Recent Advances in SELEX Technlogy and Aptamer Applications in Biomedicine. *Int. J. Mol. Sci.* 2017; 18: 11.

How to cite this article:

Kalam SA, Hashmi A and Srivastava P. Aptamers: Trending Prospective in Therapeutics. *Int. J. Res. Dev. Pharm. L. Sci.* 2020; 8(5): 1-9. doi: 10.47128/IJRDPL.2278-0238.8(5).1-9