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Review

Molecularly imprinted polymer for human viral pathogen detection

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ABSTRACT

Molecular imprinting has become an attractive synthetic approach for the fabrication of novel functional polymers with pre-designed molecular target selectivity. Such molecularly imprinted polymers (MIPs) have been applied in wide range of areas such as chemical and biological sensors, solid phase extraction and drug assays owing to their inherent robustness, reusability and reproducibility. Furthermore, MIPs can also be used as tools for studies concerning antibody/receptor binding site mimicry as well as being used as antibody substitutes for biomedical applications. Viral detection is a rapidly growing field owing to its increasing prevalence and ongoing evolution of viral variants and drug resistance. Therefore, this calls for effective detection, surveillance and control. Herein, we highlight and summarize the literature on the utilization of MIPs for human virus detection. Particularly, MIPs afford great potential for rapid virus detection as well as other recognition-based viral studies.

Contents

1. Introduction

Today, there is an apparent upsurge in the emergence and re-emergence of infectious diseases that have a major impact on the health of humans, animals and plants. In humans, infectious diseases are responsible for approximately 27% of annual deaths incurred throughout the world [1]. This reflects the combined impact of rapid demographic, environmental, social, technological and other changes in our society and habitat. Thus, there is an inherent need to develop novel diagnostic techniques so as to keep pace with the ever changing health problems that may emerge in the future.

Several detection tools are available on the market based on the concept of antigen-antibody and/or receptor-ligand interactions. In spite of their many advantages, such biomolecules possess inherent flaws in terms of stability and usage. Although a variety of bioassays and biosensors have been developed, there is still a need for low cost, disposable or reusable biosensors that are capable of rapid detection and accurate identification of a wide range of pathogens. The utilization of the molecular imprinting technology for the development of molecularly imprinted polymers (MIPs) as biorecognition elements provide a real alternative to antibodies owing to their inherent robustness and reproducibility [2]. Molecular imprinting has made it

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possible to produce tailor-made artificial receptors that are capable of binding specifically to template molecules of interests.

The molecular imprinting process essentially involves three main steps: (i) self-assembly of template and functional monomer molecules, (ii) polymerization of template-monomer complex with cross-linking monomers and (iii) template removal to unveil a binding cavity that is specific to the imprint molecule. These novel polymers have been demonstrated to possess excellent properties for the separation of many interesting compounds ranging from small molecules to macromolecules. MIPs can bind specifically to the original as well as related template molecules while also possessing tolerance to mechanical stress, temperature, pH, acid-base, etc. Owing to their robust properties, MIPs are suitable for a wide range of applications such as separation media for chromatography and solid phase extraction [3,4] nanoreactors for the combinatorial synthesis of novel enzyme inhibitors [5,6], recognition elements for biosensors [7], artificial receptors for drug assays [8,9], biological receptor mimics [10], drug delivery [11] and enzyme mimetics [12]. A wide range of templates have been imprinted such as folic acid [13], 5-fluorouracil [14], glutathione [15], gramine [16], hydrazone [17], human prostate cancer cell lines [18], matrine [19], paclitaxel [20], (S)-2-(acrylamido) propanoic acid [21], theophylline [22], uric acid [23], and valganciclovir [24]. Many viruses possess a high mutation rate thereby giving rise to new variants. A change in the antigenic epitope on the surface protein would possibly create new variants, which in turn may cause reinfection. Therefore, effective detection and control is of urgent need for proper clinical management. The inherent robustness and reproducibility of MIPs facilitate the fabrication of tailor-made receptors for rapid detection as to keep pace with emerging viral infections. This review article focuses on the surrounding literature of MIP utilization for the detection of viral human pathogens.

2. Influenza

Seasonal influenza, more commonly known as “the flu”, is an acute viral infection caused by the influenza virus. The virus spreads through an infected individuals cough thereby allowing dispersal of infected droplets into the air with the ability to infect those in the vicinity. The virus can also be transmitted through direct contact with an infected person. In addition, influenza causes an estimated 3 to 5 million cases globally with around 250,000 to 500,000 deaths annually [25]. Furthermore, the influenza virus can be classified into 3 types: A, B and C. Type A influenza viruses can be further divided into subtypes according to the combination of virus surface proteins (i.e. several isoforms of both hemagglutinins and neuraminidases) such as H1N1 and H3N2 subtypes.

Molecular imprinting polymer was first applied to screen influenza A virus by Wangchareansak et al. [26,27] as summarized in Fig. 1. This appreciated work combined MIPs and QCM for proof-of-concept of screening protocols for influenza virus subtypes including H5N1, H5N3, H1N1, H1N3 and H6N1. Influenza virus surface antigens are made up of glycoproteins hemagglutinin (HA) and neuraminidase (NA), that play a role in the subtype classification. MIPs were made for each subtype of Influenza A virus whereby each MIP possessed a good recognition property towards its original viral template. Furthermore, the template sharing the same neuraminidase domains as H1N3 and H5N3 can be differentiated by its own MIP, suggesting that the hemagglutinin domain contribute more to the selectivity property in this case. H5N1-MIP has been found to bind strongly to virus containing N1 rather than those of virus containing N3. Their finding suggests that both the H and N domain play important roles in molecular recognition of MIP. Furthermore, 5 different MIPs have been possessed as their recognition profile which are offered as molecular fingerprints. This report has opened a new feasibility providing an alternative rapid way to screen influenza A virus subtypes in unknown samples with detection limits as low as 105 particles/mL. Moreover, Wangchareansak et al. has also used the influenza virus-MIPs as a novel polymer for identifying molecular binding to the influenza virus H5N1. These MIPs were used to facilitate identification of inhibitors that can bind to, and inhibit the function of virus upon inducing a conformational change. Thus, the inhibitor treated virus is expected to have a reduced or inhibited binding to the H5N1 specific MIPs.

3. Dengue virus

Dengue is one of the fast emerging and evolving diseases in many parts of the world. Dengue is a mosquito-borne viral infection caused by dengue virus. Annually, an estimated 50 million dengue infections and 500,000 individuals are hospitalized due to dengue infection having a fatality rate of about 5% in some areas [28]. The infection can cause severe clinical problems due to non-specificity of clinical presentations leading to misdiagnosis of the disease. An effective vaccine development for the prevention of dengue is currently underway. Therefore, early detection is still urgently required for clinical diagnosis and patient management. Tai and coworkers [29,30] developed MIP for the recognition of Dengue virus protein NS1 (nonstructural protein 1). NS1 is normally found in the blood specimen during the viremia phase. It is found on the infected cell surface or as secreted NS1 in the blood. The linear 15-mer peptides derived from NS1 of JEV (Japanese encephalitis virus) was chosen as the template (Thr-Glu-Leu-Arg-Tyr-Ser-Trp-Lys-Thr-Trp-Gly-Lys-Ala-Lys-Met) according to its consensus linear epitope mapping of dengue virus NS1 towards antibody D2/8-1. This epitope-mediated imprinting based MIP was coated on QCM. The MIP-grafted 15-mer peptide chip could bind to pentadecapeptide, purified and unpurified NS1 proteins with a nanomolar range dissociation constant (K_D) of 0.6, 0.04 and 0.09 nM, respectively. The results indicated a strong polymer-template interaction from the multi-point attachment of the NS1 protein to the 15-mer peptide chip, which was comparable to the monoclonal antibody immobilized chip (K_D = 0.05 nM). Furthermore, the MIP-QCM has been applied for dengue virus detection from patients’ serum samples using the flow injection system. This MIP-QCM retained their specificity towards NS1 protein in serum and possessed high sensitivity detection down to the μM range with a short operation time of 20–30 min/sample. Therefore, this technique could be used to detect the 4 serotypes of dengue virus whereby a pretreatment sample was not needed for this novel sensor.

4. Japanese encephalitis virus

Japanese encephalitis virus (JEV) is one of the main causes of viral meningitis is Asia and Australia. Just like Dengue, Japanese encephalitis (JE) is also a mosquito-borne viral disease. The annual incidence of human cases has been reported to be about 50,000 to 175,000. In addition, JE not only has a high mortality rate (25–30%) but also reported that 50% of surviving patients suffer from neuropsychiatric sequelae. JE is considered as the most frequent viral encephalitis associated with fatal or severe outcomes [31].

The JEV recognition MIP has been fabricated based on fluorescent resonance energy transfer (FRET) [32]. The JEV recognition MIP was coated on silica microspheres which contained the fluorescent dye, pyrene-1-carboxaldehyde (PC). The FRET phenomenon can be enhanced upon virus binding as energy donor while PC acted as an energy acceptor. The novel FRET based virus detection MIP possessed high sensitivity detection of 9.6 pM at ambient temperatures. The specificity of this MIP was evaluated and found to exert an imprinting

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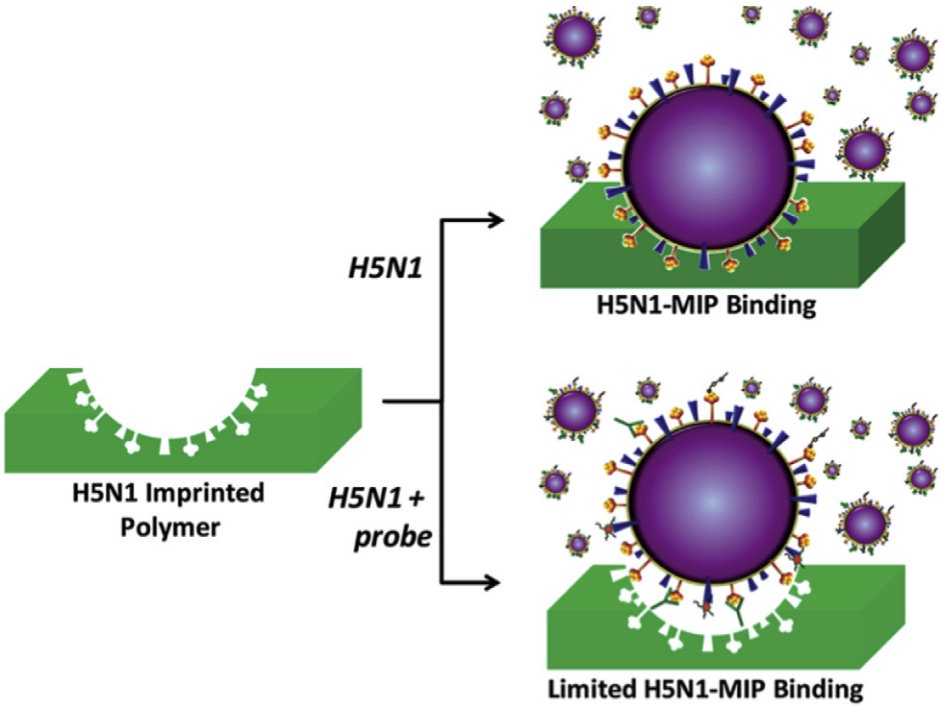

Fig. 1. Schematic representation of the binding of H5N1 virus to the imprinted polymer in the absence (right, top) and presence (right, bottom) of probe molecules (e.g. H5 antibody, Oseltamivir, Sialic acid, GlcNAc13 and H1 antibody). The binding of probe molecules to the virus causes significant conformational change which consequently, leads to limited binding of the virus with the imprinted polymer.
Source: Reprinted from [26] with permission from the Royal Society of Chemistry.

factor of 2.12. In addition, the virus MIP displayed a good selectivity towards the JEV over those of other viruses including Hepatitis A virus (HAV), Leprosy virus (LV) and Rabies virus (RV). Furthermore, its application with real samples has been demonstrated using a diluted human serum with a resulting recovery of nearly 100%. JEV-imprinted magnetic silicon microspheres were successfully invented by He et al. [33]. These microspheres exhibited excellent binding selectivity towards JEV with an imprinting factor of 2.95. Moreover, the virus-MIP possessed a detection limit as low as 0.32 nM. Furthermore, great selectivity on JEV using JEV-imprinted magnetic silicon microsphere has been demonstrated over other viruses (LV, RV). This novel MIP microsphere exhibited good recovery upon testing with virus spiked samples. Thus, JEV-imprinted polymer has great potential as a tool for application on JEV analysis and disease diagnosis.

5. Human immunodeficiency virus (HIV)

HIV primarily targets the immune system of patients, making them susceptible against other infections and certain cancers. HIV can be transmitted via various types of body fluids from an infected person, such as blood, breast milk, semen and vaginal secretions. HIV is one of the main causes of mortality and morbidity in the world. HIV has infected about 75 million people around the world and an estimated of 37 million people are currently living with the virus [6].

Lu et al. [34] has developed a HIV-1 related glycoprotein 41 (gp41) bio-imprinting sensors based on the epitope imprinting technique as summarized in Fig. 2. This glycoprotein is located on the viral coat of HIV-1. HIV-1 gp41 plays a significant role in membrane fusion upon glycoprotein 120 (gp120) binding towards CD4 cells. This membrane fusion allowing for the activation of gp41 may provide strategies for vaccine and antiviral drug development. Synthetic mimicking of a 35 amino acid residue (aa 579–613) was used as a template due to its property as a major immune-dominant region containing antibodies that recognized around 98% of AIDS patients. In this work, dopamine was used as a functional monomer. Polydopamine possessed high stability, hydrophilicity and biocompatibility. The synthetic peptide was embedded into the polydopamine during induction of the polymerization process. Hydrogen bonding, ionic bonding and hydrophobic interactions may play a role in the possible interaction between the peptide and dopamine. The hydrophobic MIP film grafted on QCM has been fabricated. The MIP coated QCM exerted a good specific affinity towards its template peptide. Upon a 100 ng/mL injection of template, the maximal frequency shifts of MIP-coated QCM sensor was 15.13 Hz whereas MIP-coated QCM sensor displayed only 1.799 Hz. The calculated K_D of this MIP was 3.17 nM, indicating a high affinity of the MIPs towards the template molecule. The selectivity of the MIP-coated QCM has been investigated against the peptide with bovine serum albumin (BSA), two and eleven mutated residues (2M-peptide, 11M-peptide). The result indicated that the BSA and 11M-mutated peptide displayed a much lower frequency response as compared to the template peptide. Whereas the 2M-peptide displayed a similar frequency response to the original template peptide. Thus the display of frequency attained by the 2M-peptide in comparison with the 11-M peptide could be due to the possible reason that it has only two mutated amino acids difference than the original template. furthermore, the whole molecule of HIV-1 gp41 has been tested to display a linear frequency shift in the range from 5 ng/mL to 200 ng/mL with a detection limit of 2 ng/mL. This detection limit is comparable to the reports from the ELISA method. The recovery performance of MIP-coated QCM towards HIV-1 gp41 urine spiked sample was in the range of 86.5–94.1%. This novel MIP-coated QCM was successfully fabricated and applied for monitoring HIV-1 gp41 in urine samples with high sensitivity and selectivity, suggesting its potential application in the future. Khaled Seidi et al. [35]proposed nanomagnet-based detoxifying machines using MIPs as viral capture for complementary approach in HIV therapy. Furthermore, the magnetic MIP behaves as a capture probe for the

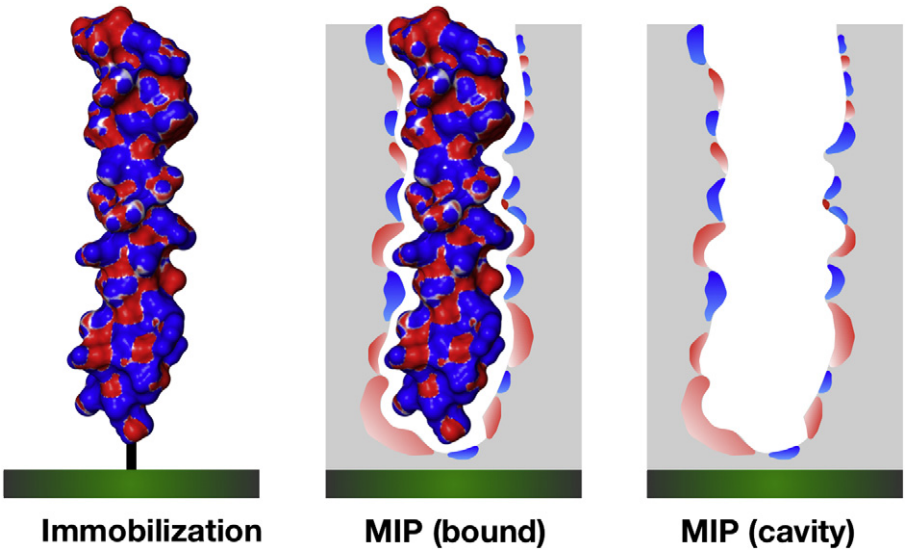

Fig. 2. Cartoon illustration summarizing the immobilization of a template protein onto a surface, formation of a molecularly imprinted polymer around the template protein and finally the elution of the template protein to reveal an empty cavity that can accommodate an incoming protein.

HIV-1 antibody that has already been invented [36]. These magnetic-MIPs have characteristically displayed a good advantage as a tool in combination with immunoassay. This MIP-combined immunosensor has also provided a low cost, simple and high sensitivity tool, which is suitable for the early diagnosis of HIV infected patients.

6. Hepatitis A virus

Hepatitis A is a liver disease caused by the Hepatitis A virus (HAV). The most common mode of infection of the disease is via contaminated food and water with feces of an infected person. Even though hepatitis A does present with chronic liver disease which is also seen in hepatitis B and C, the debilitating symptoms and sudden liver failure that accompany hepatitis A can cause death of the patient. Hepatitis A is mostly spread via the fecal-oral route and close contact with an infected person.

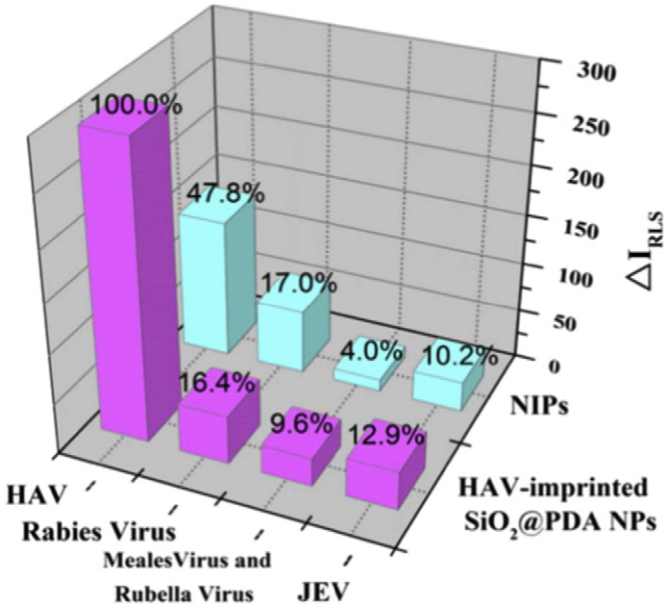

Fig. 3. Binding selectivity of hepatitis A virus (HAV) imprinted SiO_2 nanoparticles (SiO_2@PDA) towards HAV and three other viruses consisting of rabies virus, Japanese encephalitis virus (JEV) and a mixture of measles virus and rubella virus.
Source: Reprinted from [37] with permission from Elsevier.

Yang et al. [37] has applied a molecular imprinting strategy for the direct detection of the hepatitis A virus. HAV is a significant human pathogen which cannot be distinguished from other types of hepatitis viruses upon clinical presentation. Therefore, direct detection with high specificity and sensitivity plays a crucial role for accurate diagnosis. Yang developed a novel core-shell molecularly imprinted nanoparticles based on polydopamine (PDA) capped with SiO_2. This HAV-imprinted SiO_2@PDA nanoparticles possessed hydrophilic, biocompatibility and specificity recognition properties towards the HAV template. The novel resonance light scattering (RLS) technology has been employed for specific recognition and detection based on the remarkable advantage of high sensitivity and convenience in operation by using simple fluorescence spectrophotometer. The enhancement of light scattering of HAV-imprinted SiO_2@PDA nanoparticles was correspondingly related to the increasing of HAV concentration. The selectivity of HAV-imprinted SiO_2@PDA nanoparticles were tested against HAV, rabies virus, a mixture of measles and rubella viruses and Japanese encephalitis virus. The binding selectivity were in the following order: HAV was set as 100% > rabies virus (16.4%) > Japanese encephalitis virus (12.9%) > the mixture of measles and rubella viruses (9.6%) as shown in Fig. 3. This finding indicated that an excellent selectivity was obtained. Furthermore, the HAV-imprinted SiO_2@PDA nanoparticle was successfully used for the determination of HAV in real sample serum and possessed the detection limit of 8.6 pM. This novel method combined a promising technology of MIP and RLS and may open up a potential alternative way for MIPs-based virus detection.

7. Hepatitis B virus

Hepatitis B is a serious liver disease caused by the hepatitis B virus (HBV). HBV infection is the most common chronic viral infection in the world, with an estimated rate of infection of around 2 billion people with more than 350 million people serving as chronic carriers of the virus [38]. HBV infection is highly contagious and can transmit from mother to child or through exposure to infected blood.

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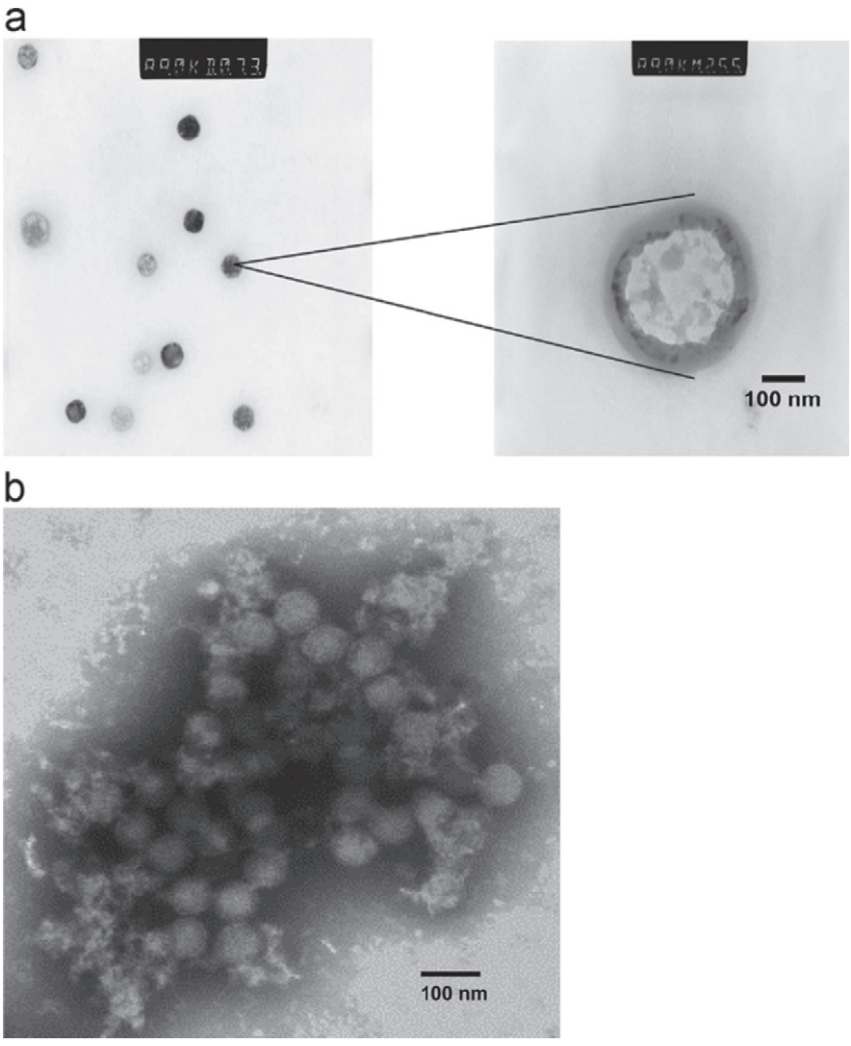

Fig. 4. Transmission electron microscope images of adenovirus imprinted polymer (a) and adenovirus (b).
Source: Reprinted from [43] with permission from Elsevier.

It is also spread by various body fluids such as saliva, vaginal, seminal and menstrual fluids. The hepatitis B vaccine is the mainstay of HBV prevention. An effective developed immunity against HBV require levels of hepatitis B surface antibody (HBsAb $\geq$ 10 mIU/mL). Uzun et al.[39,40] developed a HBsAb imprinted poly(hydroxylethyl-methacrylate-*N*-methacryloyl-L-tyrosine methylester film on the surface plasmon resonance (SPR) sensor chip for diagnosis of HBsAb in human serum and HBsAb imprinted PHEMAT particle for HBsAb purification. The prepared HBsAb-imprinted PHEMAT SPR chip displayed a good relevance of HBsAb detection which was comparable to the ELISA method (AxSYM immunoassay system, Abbott Laboratory, Illinois, USA) with a R2 value of 0.9969 linearity. The chip retained the ability to detect the HBsAb from human serum with 99.7% precision in the range of 0–120 mIU/mL. The maximum detection limit of this sensor chip was 208.22 mIU/mL with K_A and K_D values of 0.015 mIU/mL and 66 mIU/mL, respectively. HbsAb negative human serum was also tested with the PHEMAT SPR chip where no significant response was observed. Therefore, the HbsAb-imprinted PHEMAT SPR chip provides a potential use for diagnosis of HBsAb from human serum.

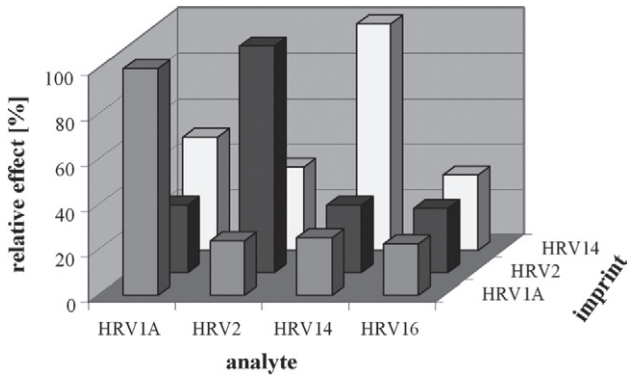

Fig. 5. Cross-selectivity of imprinted polymers against various serotypes of HRV. Imprinted polymers showed stronger rebinding to its own template.
Source: Reprinted from [45] with permission from the American Chemical Society.

8. Adenovirus

Human adenoviruses(HAdVs) can cause a plethora of clinical diseases including conjuctivitis, gastroenteritis, hepatitis, myocarditis and pneumonia. Globally, 5–7% of respiratory tract infections among children are ascribed to HAdV [41,42]. Altintas et al. [43] has fabricated Adenovirus specific-MIP nanoparticles immobilized on a surface plasmon resonance (SPR). In comparison to the MIP-based adenovirus assay, the direct and sandwich assays using natural antibodies have also been developed. MIPs were produced using glass

Table 1
Summary of experimental conditions for the molecular imprinting of human viral pathogens.

Virus	Template	Functional monomer[a]	Crosslinker[b]	Porogenic solven[c]	Format	Transducer[d]	Adsorption solvent	Ref.
Influenza virus	H5N1, H5N3, H1N1, H1N3, H6N1	Am, MAA, MMA, NVP	DHEBA	DMSO	SI	QCM	PBS pH 7.2	[26,27]
Dengue virus	15-mers peptide from JEV NS1	Am, AA, BAm	EDMA	Acetonitrile, Phosphate buffer pH 4.0	EmI	QCM	PBS pH 4.0	[29,30]
Japanese encephalitis virus	Freeze dried JEV vaccine	APTES	TEOS	Ultrapure water	MIPs coated Fe_3O_4@SiO_2 microspheres		Ultrapure water	[33]
	Freeze dried JEV vaccine	APTES	TEOS	Ultrapure water	PC-modified silica microspheres	FRET	Ultrapure water	[32]
Human immunodeficiency virus	HIV-1 gp41	PDA	PDA	Tris-HCl buffer pH 8.5	EmI	QCM	Tris-HCl pH 7.0	[34]
	HIV-1 antibody	APBA	APBA	Phosphate buffer pH 8.0	Magnetic MIPs	ECL	Phosphate buffer pH 8.0	[36]
Hepatitis A virus	HAV2	PDA	PDA	Tris-HCl buffer pH 8.5	PDA-coated SiO_2 nanoparticles	RLS	Tris-HCl buffer pH 6.2	[37]
Hepatitis B virus	Hepatitis B surface Ab	MAT, HEMA	EDMA	Toluene	PHEMAT particles		0.9% NaCl	[39]
	Hepatitis B surface Ab	MAT, HEMA	EDMA	MOPS buffer pH 6.0	PHEMAT particles	SPR	Deionized water	[39]
Adenovirus	Adenovirus	NIPAM, AA	MBAm, TBA, APTES	Ethanol	MIP nanoparticles	SPR	PBS pH 7.4	[43]
Picornavirus	HRV2, HRV14, HRV1A	PU, BPA	Phloroglucinol	Tris-HCl, THF	SI	QCM	Tris-HCl buffer pH 7.2	[45]

[a] Am: acrylamide; AA: acrylic acid; APBA: 3-aminobenzeneboronic acid; APTES: 3-aminopropyl triethoxysilane; BAm: N-benzylacrylamide; BPA: bisphenol A; HEMA: hydroxyethyl methacrylate, MAA: methacrylic acid; MAT: *N*-methacryloyl-L-tyrosine methyl ester; MBAm: N,N′-methylenebisacrylamide; MMA: methylmethacrylate; NIPAM: N-isopropylacrylamide; NVP: N-vinylpyrrolidone; PDA: polydopamine; PU: polyurethane; TBA: N-tert-butylacrylamide; TEOS: tetraethoxysilicane.
[b] DHEBA: N,N′-(1,2-dihydroxyethylene) bisacrylamide; EDMA: ethylene glycol dimethacrylate.
[c] DMSO: dimethylsulfoxide; THF: tetrahydrofurane.
[d] SI: stamp imprinting; EmI: epitope mediated imprinting; QCM: quartz crystal microbalance; PC: pyrene-1-carboxyaldehyde; FRET: Förster resonance energy transfer; ECL: electrochemiluminescence.

beads as solid support for the adenovirus template followed by the components for MIPs synthesis to obtain adenovirus-MIP nanoparticles with a size of approximately 260 nm (Fig. 4). The MIPs beads were immobilized on the SPR chip via glutaraldehyde coupling. The immobilized MIPs obtained a good reproducibility for signal detection in a concentration range of 0.02–20 pM with the detection limit of 0.02 pM. The binding affinity was calculated with a K_D of 3.10×10^{-11} using the Biacore 3000 software. In addition, the binding specificity of adenovirus-MIP was tested against the MS2-phage and vancomycin whereby non-specific binding was found in a very low level against the adenovirus-MIP. Furthermore, the adenovirus polyclonal antibody was used for direct and sandwich assays as a comparison to the adenovirus-MIP in terms of sensitivity. The K_D were calculated as 2.30×10^{-12}, 3.10×10^{-11} and 1.41×10^{-10} M, respectively, with the following order: sandwich antibody assay > MIP > direct antibody assay. The detection limit of the sandwich antibody assay was found to be the most sensitive as compared to MIP and direct antibody assay with 0.008, 0.02 and 0.3 pM, respectively. The overall results demonstrated the excellent achievement of all assay types and confirmed the suitability of the MIPs-based sensors for the detection of virus, which exerted high sensitivity and specificity as well as was easy-to-use.

9. Picornaviruses

Picornaviruses are non-enveloped, RNA viruses consisting of over 50 species in the family that can be divided among 29 genera. These viruses can reside in mammals and birds and can cause many diseases including paralysis, meningitis, hepatitis and poliomyelitis [44]. MIPs for the smallest RNA virus, picornaviruses has been developed using human rhinovirus (HRV) as a representative. Stamp imprinting procedure has been used as a template for virus-patterned memorizing geometries feature. More than 100 different serotypes of HRV were reported. Jenik et al. [45] has developed HRV-imprinted polymer coated on QCM for rapid analysis on fast frequency response shift as well as reversible non-covalent interaction behavior. The HRV2-imprinted sensor showed a frequency decrease of −750 Hz upon injection of 30 μg/mL of virus suspension whereas the non-imprinted reference channel was decreased only at −100 Hz. The frequency decrease of the sensors was dependent on the analyte concentration in linear concentration. The sensor also had the ability to distinguish between native and denatural forms of the virus. Furthermore, different serotypes of HRV in surface chemistry (HRV14, HRV2 and HRV1A) can be selectively recognized by its own HRV template origin over other species (Fig. 5). This finding confirmed the properties of this novel MIP in which it can be distinguished based upon surface chemistry even though the geometry features of template were the same. The smallest picornavirus, foot and mouth disease virus (FMDV), serotype Manissa has been evaluated for binding to HRV2-imprinted sensor. Although the geometry of FMDV was not exactly fitting due to its small size (25 nm), the surface chemistry is nearly the same to HRV. Hence, the sensor can response according to its non-covalent interactions in terms of cross-sensitivity. This work has opened up applications of MIPs for developing MIP-based virus sensors.

10. Technical remarks

Many types of pathogenic viruses have been imprinted to investigate the feasibility of various practical applications (Table 1). Various types of transducers have been utilized for fast signal recognition as

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well as increased sensitivity of detection such as QCM and SPR. Stamp imprinting and epitope-mediated imprinting have been favorably employed for governing sensing elements. Functional nanoparticles support is more straightforward upon the binding sites, which are located on imprinted surfaces for fast recognition and installation of the sensing system phenomenon such as FRET, RLS and ECL. Most of the virus template can be imprinted and cab investigate binding properties in an aqueous environment.

11. Conclusion

Molecular imprinting is an attractive technology used to create selective recognition sites within a macromolecular polymer network. One of the major advantages of MIPs is their robustness, high selectivity, long-term stability and cost effectiveness which cannot be obtained by using fragile biomolecules. MIPs have preliminarily been used for selective and sensitive viral detection as well as applied for viral subtype differentiation. Moreover, MIPs have been introduced as a novel media for the screening of inhibitors for drug discovery that may be used in the combat against viral infections. The manifold of advantages brought about by the molecular imprinting technology is anticipated to find its home in the frontlines of future viral studies.

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