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Review

Biosensors for waterborne viruses: Detection and removal

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ABSTRACT

Detection of waterborne viruses is important to eliminate and control their harmful effect as pathogens. Hence, the use of rapid and sensitive detection technologies is critically important as they can aid in investigating outbreaks and help in developing prevention strategies. To date range of viruses can contaminate drinking water sources, causing illnesses such as diarrhoea, pneumonia and gastroenteritis which can result in death. Due to their small size (nm) their complete removal from water can be difficult with current water treatment processes while being resistant to disinfectants. Available techniques for virus detection include filtration technologies, enzyme-linked immunosorbent assays and polymerase chain reaction. Although each technique has limitations, the use of biosensor technology with smart affinity materials and nanomaterials can show great potential in sensing viruses in water samples. This review reports on the latest technologies used for waterborne virus removal and detection with focus on rapid detection using biosensors.

1. Introduction

Approximately 884 million people lack access to sanitary, safe drinking water which accounts for roughly 13% of the global population [1]. This results in millions of people dying every year due to the contraction of waterborne diseases. Therefore, increasing access to safe, sanitary drinking water can significantly reduce deaths and increase global public health. Efforts must be taken to ensure that drinking water is not contaminated with harmful biological agents. Common disinfection techniques include the use of chemical oxidants (chlorination), UV irradiation and thermal treatment. Generally virus inactivation methods have not been successfully developed; currently this is due to the numerous waterborne virus strains which are not culturable *in vitro* and thus cannot be investigated and characterised. The susceptibility of many waterborne viruses to inactivation is relatively unknown because of the inability to culture these viruses [2]. Viral diseases can be preventable but unfortunately account for hundreds of thousands of deaths each year, many of them being young children under five years of age [3,4].

Viruses have diverse mechanisms of action and consist of a virion (10–100 nm) containing DNA or RNA genome encapsulated in a protein coat [5]. The function of viral nucleic acid is to carry the genetic information required to program the synthetic machinery of the host cell for viral replication whereas the capsid protects the nucleic acid from nucleases and aids in the attachment of the virus to the host cell. Viruses require a host organism to reproduce and many are pathogenic. The enterically transmitted viruses hepatitis A, hepatitis E, norovirus and rotovirus are the major causes of waterborne diseases in humans. These viruses are infectious in low doses (generally only a few virion particles are required for infection), stable in the environment for extended periods of time and difficult to study. Viruses detection in water requires specialised analytical methods and experienced personal. This combined with the detection limits of the analytical techniques used are insufficient for researchers to conclude that a sample is completely free of viruses. No known diagnostic test offers complete assurance that a sample is 100% free of viruses [6]. Also viruses are highly resistant to acidic conditions, high temperatures, disinfectants and pressure. They are intracellular parasites incapable of reproducing outside of the host's cells. Once they infect the host cells they direct the production of vast quantities of virus progeny which are excreted by the infected organism and which pose a threat to other healthy organisms [7]. The human enteric viruses enter the general water supply through contaminated sewage waste [8]. The viruses are so prevalent in sewage because infected humans excrete the viruses in enormous quantities. Persons infected with these viruses can excrete 10^5 to 10^{11} virus particles per gram of faeces. Viral infections

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are difficult to effectively diagnose and often diagnosis is only determined when the virus has spread to other individuals [9–11].

The currently available techniques for virus detection and/or removal are enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR), reverse transcription polymerase chain reaction (RT-PCR), different types of filtration techniques and biosensor technology. Although each technique has its own limitations, rapid detection methods based on biosensors provide the best opportunity since they are easy to use, cost-effective, sensitive and generally real-time detection methods. The latest developments in nanotechnology and the design and production of sensor surfaces based on synthetic materials that can be used as sensing receptors have shown great potential in achieving low detection limits for viruses sensing. In this paper, we review the trends in waterborne viruses detection.

2. Waterborne viruses

There are different types of waterborne viruses including hepatitis A, hepatitis E, rotavirus, adenovirus, norovirus and F-specific RNA bacteriophages (Table 1). Hepatitis A is transmitted to humans via the faecal-oral route or direct contact with the infected person. It mainly affects the developing world, particularly areas with poor sanitation. Vaccination is usually effective with this type of virus. Mortality rates for infection from the disease is very low, approximately 0.5% [12]. The virus enters the body via the oral route and then multiples in the intestines before spreading to infect the liver [13]. The virus is resistant to detergents, organic solvents, acidic conditions, desiccation and temperatures up to 60 °C, while susceptible to UV radiation and chlorine treatment. Infection can be reduced by vaccination, excellent hygiene and sanitation. Hepatitis E causes more severe disease than hepatitis A and is genetically unrelated to it. There are four global genotypes with the most virulent, genotypes 1 and 2, present in the developing world [3]. Outbreaks or epidemics associated with hepatitis E are attributed to the faecal contamination of drinking water [7]. The virus causes inflammation of the liver which is not fatal but results in incapacitating pain, vomiting and fever [12].

Rotavirus is responsible for a large number of diarrheal deaths especially in children. Infections with rotavirus are more frequent in the winter months and cause 5% of all child deaths annually, particularly in the developing world [3]. There are seven different groups of rotavirus which makes vaccination against it difficult [3,7] and the sanitation methods are generally ineffective [12]. Adenoviruses are responsible for respiratory, ocular, and enteric infections as well as pneumonia [13]. The viruses are difficult to diagnose as they produce few symptoms to indicate infection. Currently, human adenoviruses are classified into 54 serotypes, and placed into seven subcategories, labelled A-G [14]. Transmission mainly occurs via respiratory droplets but the virus is also transmitted via the oral-faecal route. Noroviruses are non-enveloped common agents of gastroenteritis which leads to significant fluid loss and can be fatal if adequate treatment is not provided [7,13]. Transmission occurs via fecally contaminated food and water, person to person contact, contaminated surfaces and via aerosolization making the virus highly dangerous. The virus is resistant in the environment and is especially resilient in bodies of water [12,15]. As the last group of waterborne viruses, bacteriophages (F-specific RNA bacteriophages) are naked RNA viruses with encapsulated protein capsids with a size ranging from 21 to 30 nm. The genetic codes of these phages vary in length but not significantly. Bacteriophages are viruses that infect and replicate within bacteria. They are popularly used in virus research since they are easily manipulated and are not pathogenic to humans. The phages are used as surrogates in the evaluation of the efficiency and effectiveness of water treatment systems. This is due to their small size and their similar structure to human pathogenic viruses. Bacteriophage MS2 is the most popular surrogate of these phages [16–18]. Fig. 1 shows the common schematic structures of waterborne viruses [12].

3. Separation, filtration and affinity recognition of viruses

To this day, eliminating viruses from water is a very challenging task using present-day water-treatment methods. This is due mainly to the unique properties of viruses, such as their small size making them difficult to filter (~20–90 nm), as well as their

Table 1
Properties, vaccines and diseases of waterborne viruses.

Virus	Size (nm)	Genome	Shape	Available vaccine	Symptoms & diseases	Reference
Adenovirus	80–90	Double-stranded DNA molecule	Icosahedral	No vaccine	Respiratory, ocular, and enteric infections Pneumonia, Genitourinary diseases and gastroenteritis	[12,13,115]
Hepatitis A	27	Positive-sense, polyadenylated RNA molecule	Icosahedral	Yes, vaccination is generally effective	Infection causes fever, jaundice, nausea, fatigue, abdominal cramps and anorexia	[3,13,116]
Hepatitis E	27–34	Positive-sense, polyadenylated, and single-stranded RNA molecule	Icosahedral	Available vaccine but needs to be evaluated for safety and efficacy	Inflammation of the liver which results in incapacitating pain, vomiting and fever Incapacitation of the patient	[12,116]
Norovirus	27–32	Positive sense, single-stranded RNA molecule	Spherical	No regulated vaccine; potential vaccines in phase I/II clinical trials	Vomiting, diarrhoea, nausea and abdominal pain, Dehydration, Gastroenteritis	[116]
Rotovirus	75	Double stranded RNA molecule	Icosahedral	Yes, but the variability of the different groups of viruses can make successful vaccination difficult	Diarrhoea, dehydration, vomiting and fever Gastroenteritis	[3,12,116, 117]
Bacteriophage MS2 (F-specific RNA viruses)	22.4–28.8	Single stranded RNA molecule	Icosahedral	No, not harmful to humans	N/A	[118]
Bacteriophage GA (F-specific RNA viruses)	22.7–28.9	Single stranded RNA molecule	Icosahedral	No, not harmful to humans	N/A	[17]
Bacteriophage Qβ (F-specific RNA viruses)	21.3–29.4	Single stranded RNA molecule	Icosahedral	No, not harmful to humans	N/A	[17]
Bacteriophage SP (F-specific RNA viruses)	26	Single stranded RNA molecule	Icosahedral	No, not harmful to humans	N/A	[17]