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# Detection of heavy metal by paper-based microfluidics

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ABSTRACT

Heavy metal pollution has shown great threat to the environment and public health worldwide. Current methods for the detection of heavy metals require expensive instrumentation and laborious operation, which can only be accomplished in centralized laboratories. Various microfluidic paper-based analytical devices have been developed recently as simple, cheap and disposable alternatives to conventional ones for on-site detection of heavy metals. In this review, we first summarize current development of paper-based analytical devices and discuss the selection of paper substrates, methods of device fabrication, and relevant theories in these devices. We then compare and categorize recent reports on detection of heavy metals using paper-based microfluidic devices on the basis of various detection mechanisms, such as colorimetric, fluorescent, and electrochemical methods. To finalize, the future development and trend in this field are discussed.



**Contents**



## 1. Introduction

The rapid growth of global economy and associated technological progress have caused increased environmental concerns recently (Lu et al., 2015). Heavy metals are among the most problematic pollutants as they are non-biodegradable and can accumulate in ecological systems. In case of food chain systems, they will eventually result in food chemical contamination which can lead to various diseases, threatening public health (Dai et al., 2012). For instance, cadmium (Cd) accumulates in kidney and liver for over 10 years and affects physiological functions of a human body (López Marzo et al., 2013). Therefore, accurate detection and

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large-scale monitoring of heavy metal pollution in the environment is extremely important. Many techniques have been developed for the detection of heavy metals, including inductively coupled plasma mass spectrometry (ICP-MS) (Djedjibegovic et al., 2012), inductively coupled plasma-atomic/optical emission spectrometry (ICP-AES/OES) (Faraji et al., 2010; Moor et al., 2001), energy dispersive X-ray fluorescence (EDXRF) (Obiajunwa et al., 2002), electrochemical methods (Ma et al., 2015), electrothermal atomic adsorption spectrometry (ETAAS) (Gomez et al., 2007), flame atomic absorption spectrometry (FAAS) (Sohrabi et al., 2013) and atomic absorption spectrophotometry (AAS) (Bagheri et al., 2012). Most of these techniques are of high sensitivity, specificity, and precision; however, all of them require complex equipment, professional personnel, and laborious operations (Cui et al., 2015). Thus, the detection methods that are simple, cost-effective, and portable are highly demanded especially in developing countries and areas with a lack of sufficient infrastructure, professional experts, and appropriate environmental treatment.

In the past two decades, microfluidics has emerged as a promising technology for low-cost and portable sensing applications. The majority of microfluidic devices are based on polydimethylsiloxane (PDMS), a transparent elastomer (Xia and Whitesides, 1998). However, these devices are not cheap and portable enough to be widely applied, especially in resource-limited settings. Recently, paper has been explored as a promising candidate to replace PDMS for "lab-on-a-chip" sensing and detection applications. New terms such as "paper-based microfluidics" and "paper-based analytical devices (μPADs)" have been successfully introduced and attracted growing attention recently (Li et al., 2012b; Martinez et al., 2007; Yetisen et al., 2013). The major principle of paper-based microfluidics is to pattern paper substrates into two different regions: the hydrophilic channels and the hydrophobic barriers. μPADs have several advantages over mainstream PDMS-based microfluidic devices. First, it capitalizes on capillary forces instead of extra components (*e.g.*, pumps and tubes) for flow control. Second, its cost is extremely low. In the past few years, μPADs applications have grown exponentially with many new promising technologies developed for the detection of various environmental pollutants. In this article, we summarize diverse applications of μPADs in the detection of heavy metal ions and provide insights for possible future research directions.

### 1.1. Significance of heavy metal detection

Heavy metals are often defined in literature as the metals with densities exceeding 5 g/cm$^3$ (Yetisen et al., 2013). However, this definition is arguable as it neglects all chemical properties of the substances. In this article, heavy metals are regarded as those metal elements which pollute the environment and jeopardize our food safety, such as plumbum (Pb), cadmium (Cd), mercury (Hg), chromium (Cr), copper (Cu), nickel (Ni), and zinc (Zn).

Cadmium is commonly used in industrial manufacturing and can be applied in electroplating (El-Halim, 1984), nuclear fission (McWhirter, 2013), as well as routine laboratory uses, such as helium-cadmium lasers (Harries et al., 1995). However, it can post threat to environment and humans (Nriagu, 1981). For instance, the so-called "itai-itai" disease in Japan was caused by cadmium (Bui et al., 1975). Nickel is another heavy metal that is of high importance for industrial applications. It is widely used in the production of alloys (Carroll et al., 2013), batteries (Yang et al., 2015), and plating (Shao et al., 2014). But nickel has been classified as carcinogen by various agencies and institutions worldwide (Kim et al., 2014b). Additionally, mercury has also been used in diverse applications in the past, including thermometers (Blumenthal, 1992), barometers (Peggs et al., 1979), switches (Karnowsky and Yost, 1987), and fluorescent lamps (Abreu et al., 2015). This element can cause severe problems to our ecosystem. Therefore, the usage of mercury has been significantly restricted in the past decade. Overall, to mitigate and prevent heavy metal pollution, detection and monitoring of heavy metals is an essential step.

### 1.2. Current detection methods

One of the most reliable and versatile methods of detection of heavy metals is ICP-MS. It has been developed since the 1980s (Bertin et al., 2016; Houk, 1986). For instance, Tokalıoğlu (2012) successfully determined different heavy metal elements (*e.g.*, Fe, Sr, Mn, Zn, and Pb) in thirty medicinal herb samples after microwave digestion. Moreover, an ICP-AES-based technique have been developed to detect heavy metal pollutants in wastewater (Isai and Shrivastava, 2015). Another common detection method is AAS, which is based on optical absorption. Nowadays, marine pollution has become a worldwide problem and seafood safety has played a crucial role in human health (Höfer 1998). Fatema et al. (2015) applied AAS to quantify the concentrations of Pb, Cd, As, Cr, and Hg in shrimps. Other methods, including EDXRF, ETAAS, and FAAS, are also applied (Chandrasekaran and Ravisankar, 2015; Francisco et al., 2015; Mousavi and Derakhshankhah, 2014).

Overall, current techniques have advantages in the detection of heavy metals as they are adequately sensitive, specific and accurate for the determination at trace levels (Neves et al., 2009; Saad et al., 2015). However, all of them require expensive and bulky equipment, trained personnel, and laborious operation. Therefore, researchers have been striving to develop cheap, simple, sensitive, specific, accurate, user-friendly, and environmental-friendly detection devices, and μPAD is one of the most promising solutions.

## 2. Description of microfluidic paper-based analytical devices

Modern μPADs patterned with hydrophobic barriers and hydrophilic areas can be traced back to 1902, and it was designed to prevent cross contamination between different reaction regions (Dieterich, 1902). In 1937, Yagoda and colleagues successfully created water-repellent barrier with paraffin wax in filter paper for spot tests (Yagoda, 1937). Subsequently, paraffin wax and filter paper were used for pH determination, water testing, and urine testing (Johnson, 1967; Müller and Clegg, 1949). Recently, along with the development of "lab-on-a-chip" that aims to shrink and integrate entire analytical procedures onto a single device, μPAD has extended its capabilities remarkably, including developments of immunoassays, detection of food chemical hazards and bioterrorism, urinalysis, and environmental monitoring (Maxwell et al., 2013; Zang et al., 2012, 2015). Moreover, applications of μPADs such as mixing (Rezk et al., 2012), separation (Songjaroen et al., 2012), timers (Li et al., 2013), displays (Li and Macdonald, 2016), switches (Li et al., 2008), and valves (Jahanshahi-Anbuhi et al., 2014) have also been developed in the past decade. Based on these advancements, μPADs have shown great potential for next-generation "lab-on-a-chip" devices. For instance, blood plasma separation has been successfully realized by capillary action on paper substrates with an H-shape channel (Kar et al., 2015). Albeit the separation efficiency (75.4%) is lower than conventional microfluidic chips (99.24%) (Moon et al., 2011), and it is difficult to collect the as-separated plasma from paper, μPADs still exhibited great capabilities in substitution of current chips as they require neither expensive instrumentations, nor professional personnel.

### 2.1. Properties and fabrication methods

Chromatography papers, filter papers, and nitrocellulose membranes are the most commonly used substrates for μPADs (Lu